

Manifolding For Scale-Up, Safety, And Speed

The use of manifolds to fill bags for bioprocessing or advanced therapies contributes to time savings, improved process quality, and optimal use of cleanroom and personnel resources.

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Single-use solutions (SUS) offer numerous benefits to bioprocessing and advanced therapy manufacturing. However, filling individual bags with media, buffers, cells or bulk product like viral vectors one at a time is a burdensome, time-consuming process. Single-use (SU) manifolds provide a solution by enabling seamless transition from filling single to multiple bags at once, as well as allowing for continuous, unrestricted flow of both process and product.

Implementing a new process utilizing manifolds can initially seem daunting, but understanding how implementation is accomplished, as well as how an experienced partner eases the transition, can guide organizations' decision-making on process enhancements.

Legacy Single-use Challenges

Single-use bioprocessing and advanced therapy manufacturing vary from process to process and have their own intricacies. Legacy processes typically start with a batch of media, buffer, cells, or bulk product that is required to be aliquoted into smaller sterilized bags for optimal storage and transport. This transfer is performed by linking the in-process fluid to the final bag using tubing connected by a luer or a sterile weld. After the connection is made, the product is manually pumped into each single bag, closed, sealed and stored in the optimal product environment. This procedure can be performed as an open process within a biosafety cabinet or as a closed process within cleanroom space.

Although simple to execute, this fluid-handling process requires a lot of repetition: multiple operators fill one bag at a time, and every few hours work may be interrupted by line clearances, sampling, and other mandated safety measures. In addition to being time-consuming, this process involves multiple connections (e.g., sterile welds or luers) and touchpoints to these high-value products. Each connection introduces a contamination risk, and any non-uniformity in those junctions can damage cells passing through. Further, the process is not conducive to effective scale-up for commercial-

ization, since highly skilled personnel are needed to complete each connection, and cleanroom space is both limited and expensive to expand.

Manifolds De-Risk and Optimize Production

A manifold is a collection of sterilized, single-use bags and components connected along a central line called a spine. Depending on the user's needs, different container types and sizes for storage or sampling purposes may be connected. Thus, the manifold spine allows the users to transfer a large batch of liquids to many bags at once, reducing time, process complexity and product loss from contamination. For example, filling 50 bags at a time can require sterile weld preparation of each bag before filling, with 2 to 5 minutes needed per weld. One manifold can fill those 50 individual bags all at once, reducing process time by 1 to 4 hours.

As a product scales from benchtop to commercialization, manifolds provide the flexibility to easily transition from small to large production batches. Manifold designs can range from simple to complex and can accommodate any number of final bags based on available space, process parameters, and number of operators. As product demand increases, manifolds can be used to scale up a manual filling process but can also be used when transitioning to an automated process. When making this significant transition, collaborating with an expert SU manufacturer is critical to understand the options when tolerances and budgets are tight.

Operational footprint is also a factor when considering scaling production. Fixed, limited cleanroom space can complicate technician workflows and restrict the potential of commercial production. Since manifolds provide high output within a closed system, this enables optimal use of an organization's current footprint by configuring the process around the space, rather than the space around the process.

As product demand grows, your workforce can easily multiply with it. Manifolds can provide opportunities for optimizing em-

employee responsibilities and safety. Manifolds require less hands-on work, minimizing the need for highly skilled personnel to execute filling. This leads to reduced operational downtime and simplifies and streamlines daily operations overall. No matter how the organization grows, the safety of the operators is of utmost importance. Manifolds decrease the need for multiple connections, which reduces the risk of exposing operators to bulk drug substances or viral vectors.

Manifold Implementation

As organizations discover ways to optimize their processes, such as implementing manifolds, other considerations come into play. Timelines are extremely important to project managers who are shepherding therapies or products to market. Project leaders are often wary of changes that can cause long delays, such as qualifying new components or validating new processes. Rapid prototyping of validation samples that are tested at the customer site before approval is key to tailoring a manifold to the correct process specifications. A collaborative team of single-use engineers can reduce complications that lead to delays, alleviating stress while ensuring process requirements can be met when manifolds are added to the process. Ultimately, this enables speedier time to market so therapies can get to patients quicker.

The cost of manifold implementation is just as critical as a shortened timeline, since cost-effective implementation is vital to a product's short- and long-term viability in the market. Organizations tend to implement manifolds while operating in early-development phases. At this stage, revenue is not being generated and the motivation to limit capital investment is high. Cost savings primarily are realized in the longer term, manifesting from reduced operating costs as processes scale. Early manifold implementation can continue to streamline cost and efficiency as commercial production expands.

A third critical factor to bioprocessing and advanced therapy manufacturers is working

with a supplier with a robust supply chain. Developing a long-term customized solution requires a secure supply chain for all materials within the design. The ability of a partner to meet process-specific requirements with single-use materials calls for transparency regarding the availability of supply, as well as challenges to its procurement, and should be discussed before implementation. An expert partner will serve its customers by collaborating with their teams to appropriately implement manifolds into their process based on process parameters, timelines, cost, and supply while understanding their end goal.

Final Thoughts

The use of manifolds to fill bags for bioprocessing or advanced therapies contributes to time savings and improved process quality, as well as optimal use of cleanroom footprint and skilled personnel. Moreover, manifold design, development, and usage can be adopted into many organizations' manual processes, reducing the need for costly automated system purchases and implementation as products grow.

Manifold implementation is a collaboration that requires customers to have a clear understanding of their needs. It also requires customers to understand which elements of their biomanufacturing processes could be optimized for better results. A knowledgeable SU supplier can provide insights that guide an inexperienced customer through this process by introducing perspectives that might otherwise have not been considered.

Successful collaborations begin with having the right people present during initial conversations, including hands-on individuals who are familiar with the process, like lead scientists, and process engineers. To learn more and start the conversation, visit <https://chartermedical.com/regenerative-medicine/manifolds/>

Additional Resources

Custom Product Design - Charter Medical

About The Authors

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About Charter Medical, LLC

Charter Medical, LLC has more than 30 years' experience developing and providing specialty single-use products for bioprocessing, advanced therapies, and blood management applications delivering solutions to the biotechnology and pharmaceutical markets.

Our 16,000 square feet of cleanroom space located in Winston-Salem, NC, is ISO 13485 certified and FDA registered, with a focus on designing and supplying single-use solutions for cell growth, frozen storage, and biological fluid handling. Custom product design services are available for clients who need specialized single-use products for biomanufacturing. Our team of engineers will work with you to develop the best solution for your specific requirements.

Charter Medical is committed to providing quality products and services with an experienced staff dedicated to exceeding customer expectations from product development to delivery and implementation.

Charter Medical works closely with our sister companies, Secant Group and SanaVita Medical, to provide essential products and services to life science companies. Through integrated research and development activities, we are helping to bring new technologies and therapies to market.

