Single-Use Systems: The Future of Biopharmaceutical Processing

Testing of tubing ensures that products are suitable for high-risk applications, such as drug-delivery devices, combination products, and long-term implants.

Single-use systems represent the future in biopharmaceutical processing of therapeutic drugs with significant advantages over traditional reusable stainless-steel systems and partly disposable systems. Seemingly the antithesis to a whole world trying to move away from disposable products and processes, Single-use systems promote sustainability by eradicating the chemicals and resources, like water and energy, needed to sterilize reusable systems. Perhaps, most importantly and critically, this is with little cost and process time, and virtually eliminates the risk of cross-contamination, since the product flow path is discarded and replaced after each batch.

MANUFACTURING PROCESS SYSTEMS

Within the biopharmaceutical industry, three types of processing systems create therapeutic drugs. The first type involves stainless-steel systems. These are reusable, durable, and able to withstand exposure to the chemicals used to sanitize pharmaceutical processing systems, usually at extreme temperatures. This necessitates stringent sterilization regimes potentially involving harsh chemicals and steam, resulting in considerable energy consumption to bring systems up to the extreme temperatures required for effective sterilization.

Biopharmaceutical companies utilize a single-use system to manufacture vaccines using large scale bioreactor bags.

The second type is partly disposable systems. These utilize some parts of the processing system more than once, depending on the therapeutic produced. Reused parts undergo cleaning and sterilization regimes like those used in stainless-steel systems, and maintenance is required as reusable elements deteriorate over time. Both stainless-steel systems and the reusable parts of disposable systems have the inherent risk of contamination, even with validated cleaning and sterilization programs.

Single-use systems, the third type of bio-pharmaceutical processing system, are designed for use for the duration of the production process of a single batch of therapeutics and then discarded. The rise in the adoption of single-use technologies is proving to reduce product crosscontamination risks by eliminating the need for cleaning between batches. Manufactured in a cleanroom, double bagged and then sterilized by gamma, EtO, or x-ray sterilization methods, these systems ensure a sterile system for every batch, as well as being highly efficient and cost effective.

According to a study conducted by Single Use Support GmbH, single-use systems lower operating costs by offering 46 percent water and energy reductions, a 35 percent more favorable CO_2 footprint due to lower facility emissions, and a 40 percent lower initial investment cost. They allow pharmaceutical manufacturers to push products to market faster by increasing throughput and making scalability easier.

THE SHIFT TO SINGLE-USE SYSTEMS

Single-use bioprocessing systems have gained significant traction due to the rapid adoption of disposable technology by pharmaceutical manufacturers. According to Allied Market Research, the

value of the global single-use bioprocessing market was $2,800 million in 2016, and the projection is for it to reach $9,342 million by 2023; at a CAGR of 18.7 percent over the period.

The technology is primarily applied in the manufacture of biologics both in the upstream, including bioreactors (see the sidebar, “Customer Collaboration for Engineered Solutions”), media preparation, buffer preparation, and downstream processes of manufacturing, including fluid path transfer for filtration, chromatography, viral clearance, and other steps. Common therapeutics produced with these methods include monoclonal antibodies, mRNA vaccines, and other pharmaceutical components on a commercial scale. However, there are challenges in developing these systems relating to gaining regulatory approval of component materials, navigating the nuances of material compatibility with process fluids, and maintaining the supply chain. For these reasons, suppliers must provide assurance that their products deploy operational best practices and are certifiably and regulatorily safe.

A BRIEF OVERVIEW OF BIOPHARMACEUTICAL DRUGS

Biopharmaceuticals include a wide range of products, such as vaccines, therapeutic proteins, blood and blood components, and tissues. In contrast to small molecule chemically synthesized drugs, which have a well-defined structure, biopharmaceuticals derive from living materials (human, animal, microorganism, or plant) and are much larger and more complex in structure.

Because biopharmaceuticals work with the immune system and do not contain chemical-based drugs, there is a rapidly expanding acceptance of biopharmaceuticals to treat a range of diseases, and the market is growing quickly. In addition, an increasing aging population in Western countries, rising costs of healthcare globally, widespread presence of chronic ailments, technological advancements, and manufacturing and contamination factors are all driving the rise in biopharmaceutical market demand.

The biopharmaceutical method of making drugs is an especially high-profile topic due to the global COVID-19 pandemic and the use of the mRNA vaccine, which is made using the biopharmaceutical process.

VALUE OF QUALITY AND MATERIAL EXPERTISE

When utilizing a stainless-steel system, after biopharmaceutical manufacturers produce a batch of drugs, they must clean and sterilize all the equipment to prevent cross-contamination and ready the equipment for the next batch. This can be a costly and time-consuming process, and the risk for contamination remains.

In single-use systems, all process parts, including hoses, bags, and seals, are disposed of, and replaced with a new set, so the system is quickly back up and running. This saves time and money, involves less risk of contamination, and generates greater throughput. An experienced supply partner can provide manufacturers with all the data that supports the quality of the component materials and parts requirements. This may include production of parts in a cleanroom and independent laboratory testing.

There are two main bodies of regulation impacting components used in single-use systems: material biocompatibility and leachables and extractables. Biocompatibility looks at the material used in the component and whether there are any harmful reactions or long-term bodily effects caused by chemicals. Biocompatibility testing requirements fall within USP 87, USP 88, and ISO 10993

depending on the application, while extractable and leach-able tests run on the finished products used in single-use systems. These requirements fall within USP 665 or the BioPhorum Operations Group (BPOG) Extractable and Leachable protocol.

The BioPhorum Group is an industry group leading the development of new best practice guides for single-use systems. This is stimulating the development of standards and guides by other organizations, such as ASTM-BPE, PDA, and ISPE. BPSA guides cover irradiation and sterilization validation, determination of extractables and leachables, and disposal of single-use systems.

EXTRACTABLES AND LEACHABLES

To select processing materials that avoid risk, it is important to understand the chemical nature of extractables and leach-ables. *Extractables* are compounds emitted from a packaging component, delivery system, or manufacturing surface during aggressive testing. *Leachables* are compounds that migrate into the drug over time from contact with the system componentry and manufacturing surfaces.

An interaction of extractables or leach-ables with drugs or other media can be harmful to individuals and have possible long-term effects on the human body. Thorough testing ensures that products are suitable for high-risk applications, such as drug-delivery devices, combination products, and long-term implants. For example, extensive tests conducted by Trelleborg experts determine the extraction levels of substances under different conditions. Results show that Trelleborg's tubing and hoses meet the highest standards and demonstrate outstanding purity levels.

CUSTOMER COLLABORATION FOR ENGINEERED SOLUTIONS

Trelleborg supported an international biopharmaceutical producer on an advanced development to address the challenges of using a single-use system within a bioreactor. The customer wanted to scale up its bag system to a total volume exceeding 2,000 L. The aim was to retain the proven geometry and impeller design of smaller-scale systems, as well as the tip speed and power input per volume.

One of the difficulties encountered with this was the much higher force that the assembly had to withstand compared with other smaller-scale bioreactor bags. On a scale-up of this size, the mixer inside the reactor receives a huge amount of torque. Therefore, the customer needed a new drive assembly for the mixing technology inside the bag and called upon Trelleborg to help provide a solution.

Trelleborg experts recommended an entirely new self-contained unit, designed specifically to the client's specifications. The team proposed a radial magnetic coupling using an assembly incorporating a special bearing.

Welded on the bag, the complete assembly, consisting of the radial magnetic coupling and a polyethylene port, ensures hermetical sealing between the bag and the external environment, eliminating the risk of contamination and maintaining a sterile barrier.

The first coupling design with ceramic bearings shipped after only 12 months, with the second design, made of ceramic and polymer bearings, following not far behind. Manufactured entirely from machined components, assembly of the scaled-up design was in a cleanliness-controlled environment.

The radial magnetic coupling proved to be very stable with no rocking or tilting, even when subjected to high forces. The final design has a bag diameter of around 4.25 ft and a height of 7.5 ft, resulting in a complete surface area of around 140 sq ft. Following two years of successful trials at the beta site that confirmed the biological performance and mechanical robustness of the new product, the 2000-L bioreactor bag is now in mass production.

CONCLUSION

Single-use bioprocessing technology has gained significant traction due to the rapid adoption of disposable bioprocessing equipment by pharmaceutical manufacturers. These systems help manufacturers save time and money while minimizing the risk of contamination. Additionally, pharmaceutical manufacturers can select processing materials that limit extractables and leachables and rest assured that they meet all regulations by partnering with an experienced components supplier.

By monitoring the market and staying in tune with customer needs, components suppliers can help therapeutic manufacturers choose the right material for the right application. When components suppliers have global reach and material development expertise, they can demonstrate a comprehensive understanding of product applications. This allows them to collaborate with therapeutic manufacturers to understand their needs and provide the best solution.

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