Trends, Opportunities, and Challenges in Single-Use Systems

Continuous manufacturing is a growing focus and is expected to prevail in the next 10 years, a prediction that impacts the design and performance requirements of single-use systems and their components.

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Approximately 85 percent of pre-commercial biopharmaceutical manufacturing is completed with single-use systems (SUS) and the biopharmaceutical industry has seen 14-15 percent consistent annual growth over the last decade.

As the industry gains experience and confidence in utilizing these materials, SUS have become indispensable tools in the development and optimization of biopharmaceutical processes to protect against contamination, increase flexibility, and eliminate costs. This trajectory will continue to rise as the need for efficiency and cost savings in drug development and manufacturing processes increases.

Trends Impacting the Biopharma Industry

Biopharma manufacturers seek universal solutions and standardized data to accommodate industry-driven protocols. Standardized protocols across component suppliers provide the opportunity for better comparability and accelerated risk assessment analysis for manufacturers. Specifically, this includes more relevant standards to test for particulates, extractables, bioburden, and integrity that are designed for SUS and other components.

The ability to provide improved and more relevant data allows end users to rely on supplier-generated data on supplied components to mitigate risk and accelerate implementation during the validation of single-use components.

The dataset allows manufacturers to demonstrate the performance, quality, and purity of product solutions, reducing the need to invest time and money for the end user to test each material themselves.

Enhanced traceability throughout the entire supply chain is vital to ensure proper equipment usage and eliminate the possibility of errors in the production stage.

An integrated supply chain is an important element of traceability as it allows control over each...
process, from the synthesis of the starting monomers and the basic silicone polymers down to the extrusion into the tubing and the manufacture of over-molded assemblies. This helps create high-quality products that are clean, pure, reliable, and consistent.

A unique advantage of a supplier with vertical integration for tubing is privileged access to and control within the entire supply chain with traceability at every step of the manufacturing process, and an exceptional change control process.

**Challenges in Extractables and Leachables**

Like any new technology, single-use systems come with a unique set of challenges. One potential concern is the presence of extractables and leachables. Extractables from silicone tubing are low levels of low molecular weight oligomers originating from the silicone polymers.

The extrusion process and manufacturing environment also influence the extractable profile of the end-product. Expertise of both material science and extrusion process can improve extractable levels.

Extractable and leachable concerns apply mostly to the process contact materials (PCM) components, especially in the downstream part of the biopharma process after the filtration step. Tubing, as well as bags, are among the largest surface components in contact with the final drug and should demonstrate a low extractable profile.

Silicones offer one of the cleanest purity profiles compared with most thermoplastics, reducing the concern of extractables. However, there is increased concern with the use of non-silicone materials, like polyvinyl chloride and other thermoplastics, where tubing manufacturers have less control within the upstream value chain as it is more fragmented and focused on large-scale manufacturing for industrial application. Consequently, it offers less traceability and healthcare regulatory compliance.

The extractables profile of Pt-cured silicones are simple and predictable because there are no organic additives introduced into the formulation, and there is no by-product formed during the curing reaction. Silicone materials should not be utilized in cases where the material is exposed to extreme high or low pH conditions for a long period of time.

These conditions can slowly break down the siloxane backbone of the silicone materials and cause the degradation of the tubing. It is well known in the industry that silicones swell in non-polar solvent and absorb non-polar preservatives into the tubing wall. Process parameters, such as shorter contact time, need to be adapted to overcome these potential challenges.

Extractable testing information is important for the implementation of single-use
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components and systems and for risk assessment of the potential impact on drug substances and products. However, testing packages across suppliers are inconsistent and incomplete.

For this reason, the BioPhorum Operations Group (BPOG) developed a standardized protocol for generating extractables data that would meet the end user requirements and simplify and reduce implementation time.

Concerns in Long-Term Operation Changes

Continuous manufacturing is a growing focus and is expected to prevail in the next 10 years, a prediction that impacts the design and performance requirements of single-use systems and their components. These long-term operation changes present a variety of challenges for SUS, including:

- Chemical compatibility of the material of construction of the single-use components with a drug: Silicones are an excellent material of choice as they are resistant to many commonly used chemicals in biopharma processing.
- Pressure resistance: Silicone tubing can be produced in a wide range of durometer (up to 80 shore A). Pressure resistance can be adjusted by the formulation of the silicone tubing, or the tubing wall can be reinforced by fibers.
- Longer durability silicones keep their physical structure and performance and resilient properties longer than most of the thermoplastic elastomer (TPE) tubing. Silicones are very resilient and most commonly used in peristaltic pumps, but over a longer period of pumping applications, depending on the pumping conditions, they start to spall (flake).
- Biofilm build-up: Silicones have hydrophobic surfaces that limit biofilm formations.
- As continuous manufacturing continues to gain traction, partnerships between suppliers and drug manufacturers will be imperative to ensure correct implementation of SUS to facilitate new operation processes with suppliers.

Building Strong Partnerships

The maturity of SUS in biopharmaceutical processing provides new and exciting opportunities for manufacturers to increase productivity, cut costs, offer complete traceability, and eliminate contamination. For ease of implementation and to alleviate challenges, it is vital for drug manufacturers to partner with trusted component suppliers. This allows companies to share part of the complexity and responsibility with suppliers to uphold consistency and quality standards, maintain a vertical supply chain, and generate standardized data.

Two-thirds of bioprocessing professionals expect at least 50 percent of substantial unit operations to rely on single-use system devices¹, suggesting that manufacturers will need more comprehensive data packages to integrate SUS, and to maintain close contact with their selected partners to ultimately tap into the full potential of SUS.

About the Authors:

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