Building Reliability Into Bioprocessing – How Component Testing Improves Consistent Performance

By

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Cost of failure has been a consistent topic in bioprocessing for decades, yet the industry still has significant challenges with manufacturing robustness. Bioprocessing manufacturers work to ensure reliability through evaluation of single-use system (SUS) assemblies and individual components, and maintain a presence for suppliers through their evaluation and product qualification process as they perform their due diligence in verification and validation of performance.

SUS components need to undergo a battery of tests to check that they are robust, easy-to-use, and reliable. They must be biologically and chemically compatible with liquids used in and around bioprocessing, while able to handle temperature and flow rate requirements. From sterility to freeze/thaw resistance to bubble leak testing, each test can offer insights into how well a component will function in the user's particular application.

While a bioprocessing manufacturer may believe that every SUS component on the market undergoes a similar degree of rigor in its testing, the types and precision of these tests can vary widely between suppliers. For those manufacturers, determining the best products to incorporate into single-use systems requires an understanding of both the process specifications and the component's capabilities.

Vetting suppliers for their testing facilities, procedures, and documentation practices helps bioprocessing manufacturers evaluate SUS components and whether they could be the right fit for their application. Bioprocessing manufacturers should expect component suppliers to, at a minimum, validate performance and readily provide the validation package to support end-user adoption.

VALIDATION TESTING FOR BIOPROCESSING APPLICATIONS

Because of the wide range of potential applications, single-use aseptic connectors used in SUS come in a variety of configurations – from 1/8" microconnectors to 1" large volume connectors, from male/female to genderless, from standard to custom. These components must be optimized to maintain the integrity of the overarching manufacturing process. To achieve this, suppliers should engage in an array of testing that both simulates and exceeds manufacturing conditions, including several core tests that form a comprehensive validation model.

Reliability starts with building the test plan. Colder Products Company's (CPC) product development teams work with integrators and end-users to understand the expected life cycle for their SUS components. By creating this framework, the teams are able to develop a test plan that mirrors predicted sterilization exposures, temperature induced stresses, and physical load induced stresses. From manufacturing to shipping, assembly to sterilization, and storage to usage, the wear and tear that a component can conceivably experience can be staggering.

Among the other tests CPC performs are accelerated aging, shipping and vibration, flow and burst, and biocompatibility testing to assess product durability and integrity. The testing profiles of its various components are available to biopharmaceutical manufacturers so they can evaluate components for integration in their manufacturing applications.

Bacterial ingress testing is one of the most important foundational tests for a single-use component. Sterility is

essential in manufacturing a biologic, cell therapy, or gene therapy, and maintaining a sterile fluid path from start to finish relies, in part, on the connectors that link that fluid path. When a manufacturer joins two or more separate systems together, maintaining the sterility of each system and the connection between them is critical. Compromising sterility means compromising the entire manufacturing process and product. Sterility breaches create the potential for delays, rework and product loss.

At CPC (Colder Products Company) this bacterial ingress testing is performed by dipping or submerging the ends of a connector in a microbial challenge bath. Both sides of the connector are exposed to this microbial challenge bath in a laboratory then connected to two sterile systems. After a connection is made, liquid growth media is moved through the systems to simulate the manufacturing process. The liquid is subsequently tested to ensure that none of the challenge organism that the connector was exposed to was able to enter the sterile system.

In submersion bacterial ingress testing, a fully assembled connector is submerged in the challenge liquid, after which growth media is flushed through the connector. For this test, components are pre-sterilized using gamma radiation or autoclaving, and are tested after a seven-day incubation period once exposed to the challenge bath and flushed with growth media.

Pressure and temperature tests are other important tools in validating components for use within specific applications. At CPC, bubble leak testing is performed prior to and following these tests to verify the integrity of these components in a variety of temperature and pressure conditions potentially found in certain bioprocessing applications. CPC also uses custom equipment that simulates real-life product handling in the lab and field. Another key assessment for components utilized for bioprocessing are bioburden and endotoxin particulate tests, which are designed to validate that components are free of a range of living organisms (bioburden) and gram-negative bacteria (endotoxins) that could compromise a system.

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CPC'S VALUE PROPOSITION FOR BIOPHARMA

CPC's testing facilities are best-in-class among component suppliers. Its engineers leverage advanced modeling capabilities and prototyping equipment to evaluate the performance of every design, and are equipped to develop and test custom components based on individual customer needs. Additionally, CPC can offer verification testing of customers' own bespoke component designs, streamlining the approval process and facilitating faster market acceptance.

CPC has also invested significantly in its testing facilities and expertise in response to growing industry demand for single-use systems and aseptic connectors. In-depth fluid flow analyses further characterize the functional capabilities of its products and technologies. CPC has also devoted extensive resources in the mechanical side of its testing, facilitating more comprehensive evaluation of the physical limitations and robustness of its products.

CPC's commitment to holistic product validation is evidenced by its qualification plan for new components. These plans combine a range of rigorous evaluation metrics, such as functional testing, verification testing, and risk assessment, to meet a customer's expectations and required outcomes.

End users are responsible for evaluating the functionality and performance characteristics of a connector or component before integrating it into a bioprocessing application. CPC, a global leader in single-use connection technology, has pioneered testing processes that offer users a comprehensive understanding of its products. This focus, coupled with making a number of its product testing profiles available, position CPC to support biopharma, cell therapy, and gene therapy companies to implement and scale their processes seamlessly and confidently.

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