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The Advantages Of Blow/Fill/Seal Processing For Vaccine Production

Source: Weiler Engineering, Inc.
By Marty Reyes, Weiler Engineering

Traditional vaccine production often includes an equally traditional vessel for end products: multi-dose glass vials, which have served as the standard for many drugs for decades. But the use of glass vials creates a number of challenges for manufacturers and providers alike — a shortage of glass in some countries, coupled with the potential for contamination in both the manufacturing process and the drug's administration, make the use of these vials an increasingly outmoded practice. Other factors, such as the potential for human error in administering the correct dose, can make single-dose vessels a more attractive option for pharmaceutical companies. This has led to recognition among regulators that advanced aseptic processing techniques like blow/fill/seal (B/F/S) offer greater safety and customization for drug product manufacturing.

In the B/F/S process, thermoplastic resin is melted and formed into a parison that is treated with sterile air, sealed at one end, filled with drug product, and hermetically sealed at the other end to form a discrete single-dose container. This end-to-end process, once initiated, occurs with little to no human intervention needed, greatly reducing the potential for contamination. It also allows for a wide range of container designs and product volumes, creating flexibility and ensuring greater end-use safety for patients. Executed under controlled conditions, B/F/S includes five basic steps:

1. **Extrusion**: A thermoplastic resin is extruded as a hollow tube known as a parison.

2. **Parison cut**: When the parison reaches the proper length, the holding jaw and main mold close. This pinches the bottom of the parison while the top is held in place as the cutting sequence occurs.
3. **Blow and Fill**: The blow/fill nozzle is inserted into the parison, forming a seal with the neck of the mold. The nozzles blow sterile, filtered, compressed air or nitrogen into the parison to expand it before venting the air out. The sterile product is then deposited into the parison through the fill nozzle.
4. **Seal**: Separate sealing molds close to form the top, which hermetically seals the container.
5. **Release**: Finally, the mold opens, and the formed, filled, and sealed containers are conveyed out of the machine.

These multicomponent filling and sterilizing systems represent unique advantages for vaccine production, particularly in the face of the COVID-19 pandemic and the resulting global response. With appropriate changes to process parameters, these systems can be adapted for vaccine production without incurring any product degradation, and their widespread implementation can be achieved through adaptive strategies centered on experience, scientific principles, and long-term, global strategies.

Glass vs. B/F/S: The Next Generation of Aseptic Processing

One of the challenges inherent to employing multi-dose glass containers is in the potential for breakage — during the manufacturing process, in storage, during transportation, and at every point in between. The weight and dimensions of glass containers create particular challenges for storage and transport, and special considerations surrounding cleanup and remediation for breakage that occurs during manufacturing can create production delays. Because these vials are created with only a limited range of cylindrical designs and are heavier than plastic containers, the logistics of global distribution become more complex and less agile, contributing to additional costs related to the weight and volume of the containers utilized in transporting them.

Global regulations demand a safer, more flexible means of vaccine distribution. Manufacturers can fully customize the size and shape of B/F/S containers, allowing companies to explore novel designs that maximize utility, create storage efficiencies, and encourage ease-of-use for providers. The tightly controlled nature of B/F/S creates a fully automated, self-contained process that greatly reduces the potential for contamination. In it, a container is created under ISO 5 (Class A) aseptic conditions in a matter of seconds, all without the need for human interaction, eliminating the potential for bacterial contamination. Glass vials, in contrast, are filled with much more human intervention and present additional challenges regarding particulates introduced by either glass delamination or the process environment. Mitigating this potential for contamination creates additional costs and is almost always reactive, as it translates to additional testing throughout the manufacturing process to detect contamination.

In contrast, B/F/S virtually eliminates the potential for contamination by removing its primary source: manual handling during the manufacturing process. Because B/F/S systems are fully automated, with completely integrated clean-in-place and steam-in-

place processes, several industry experts have declared B/F/S to be approximately 100 times lower risk than traditional glass filling.

Addressing Concerns of Transitioning to B/F/S

Typically, the high-temperature extrusion process in B/F/S offers greater quality assurance with regard to sterility. For vaccine production, however, concerns surrounding the impact of heat on the product must be addressed with careful planning and process workarounds. Ultimately, B/F/S can be implemented in vaccine production by altering process parameters without compromising the quality of the drug product or the sterility of the packaging.

As with any process transition, switching to B/F/S from more traditional filling methods represents a capital investment that may serve to disincentivize pharmas or even CDMOs. But that initial investment is relatively low and is counterbalanced in the long term by savings realized by a lower per-unit cost of production. Despite this, many pharmas or CDMOs may have lingering concerns surrounding their processes and adapting them to B/F/S filling. This is another concern best mitigated with experienced CDMOs or technology providers that can help pharmas establish the right parameters for their vaccine to maximize its safety, transportation, and storage potential.

B/F/S technology has been around for several decades and has seen marked success in several key drug product arenas, including biologics and protein production. The historical dominance of multi-dose glass vials in the market, however, has resulted in a relatively slow adoption of B/F/S in the U.S. as compared to European and Asian countries. It is still much more common to see injectable products produced with B/F/S in the European and Asian markets, but that paradigm is shifting as glass becomes harder to secure, and B/F/S continues to prove its superior sterility and applicability across a wide range of drug products, including vaccines.

Choosing a Partner in B/F/S Filling

At Weiler Engineering, Inc., we work to continuously innovate on technological advancements for the equipment designs and systems we provide our customers. With more than 60 years of experience with advanced aseptic processing technologies, Weiler guarantees its customers the highest level of quality for their sterile liquid products. By offering six different B/F/S machines of different configurations and specifications, each one adaptable to a project's unique process parameters, Weiler is able to provide its customers with equipment tailored to their manufacturing needs regardless of the size and scope of a project. Models like the ASEP-TECH® Model 640 offer clients a wide range of potential container volumes, from 0.2 ML to 1,000 ML, as well as the capability to produce several different volumes in a single mold set. This flexibility affords clients a wide range of container designs previously difficult to source or unachievable through traditional sourcing channels.

Beyond its experience with biologics and proteins, Weiler has helped to implement its B/F/S processes for vaccine production, affording it an experience few others in the U.S.

can claim. In February of 2020, GlaxoSmithKline (GSK) began distributing its Rotarix vaccine in Myanmar, the first rotavirus immunization in the country. The Myanmar project also marked the first time a B/F/S container was used to administer the vaccine, which was produced using B/F/S technology provided by Weiler.

Ultimately, implementing B/F/S technologies for vaccine production offers several advantages over traditional glass vials, particularly with regard to sterility and safety for patients. The ability to quickly and easily produce single-dose containers and tweak their design for optimal storage and transport makes B/F/S a great choice for vaccine production, which continues to ramp up as the U.S. moves toward a more global response to the pandemic. Through partnerships with experienced aseptic processing technology providers like Weiler, pharmaceutical manufacturers and CDMOs can easily adapt their processes to accommodate B/F/S, realizing long-term cost savings and improved product quality for their injectable products.

About the Author

Marty Reyes is the Sales and Marketing Director with Weiler Engineering, Inc. He has over 36 years of experience in the Blow/Fill/Seal community. His experiences in technical roles include Research and Development, Technical Support in Contract Manufacturing plant operations, and Global Technical support to all Weiler Engineering Customers.

About Weiler Engineering

Weiler Engineering, Inc. provides advanced aseptic liquid processing technology through the application of customized ASEP-TECH® Blow/Fill/Seal machinery and integrated services that include development for customer-specific applications. Since 1959, the company has brought innovation in design, development, technology, validation, and regulatory science to each project. Weiler is committed to the highest standards of excellence and to further expanding its products and systems to enhance patient care. www.weilerengineering.com.

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- Government Partnership Highlights Blow/Fill/Seal Advantages In Race For COVID-19 Vaccine

  Continued global efforts to incorporate B/F/S in the safe and efficient delivery of life-saving vaccines are proof the technology serves as a valuable tool in improving patient care across the world.

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