apijectTM insights

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Blow-Fill-Seal (BFS) Covers Injectables and Vaccines, Too

BFS drug delivery systems go far beyond ophthalmics and oral solutions; BFS is also used to fill-finish injectables, including vaccines

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Ray Sell has been active in the contract pharmaceutical industry for almost 25 years, holding a wide range of roles at companies including Catalent Pharma Solutions, Bellwyck Pharma Services, PCI Printed Components, Cardinal Health PTS, and most recently PCI Pharma Services where he served as Director, Business Development, CDMO North America.

Many pharmaceutical company executives are familiar with Blow-Fill-Seal (BFS) as an aseptic fill-finish technology. They know BFS is used for over-the-counter products such as ophthalmics and oral solutions.

But some are surprised to learn that's just part of the story.

BFS is also a proven and widely accepted way to package many different products – far beyond oral solutions and ophthalmics -- including biologics, some vaccines and more than 50 injectables. Most of these products are distributed in BFS outside of the U.S.

Perhaps the most important thing to know about BFS is the reason why the FDA calls it an "advanced aseptic process" in its 2004 Guidance statement. That's because BFS is highly automated; very little human interaction with the drug occurs during the BFS fill-finish process. Since there is minimal opportunity for drug contamination by human interaction, BFS offers alternative to traditional fill-finish methods.

Part of our initiative here at ApiJect is to work with global pharmaceutical companies that will file BLA (Biologics License Applications) with the FDA, relevant to their drug or vaccine in our BFS Container, in conjunction with the 510(k) clearance that ApiJect is seeking for its Needle Hub and

(continued)

Connector. The combined device will then go down a regulatory approval submission path in the U.S. (Note: The Needle Hub and Connector of ApiJect's Prefilled Injector has been submitted for review but has not been cleared by FDA or other regulatory authorities.)

Arguably, until ApiJect arrived on the scene, there may have been little reason for pharma companies to know about the potential to use BFS as a prefilled format for injectables.

A common misconception about BFS is that storing biologics in plastics is a problem that could lead to leaching or extractables. Bulk API can be stored in large plastic containers at some point in the life cycle, before being transferred into glass vials or some other container.

An Intermediate Bulk Container (known as an IBC) is defined as a container used for transport and storage of fluids and bulk pharmaceutical materials. The construction of the IBC container, and the materials selected for use, depend on the application or the product itself whether it's a vaccine, a therapeutic or other drug substance.

Various types of IBCs are on the market including plastic or composite, as well as stainless steel. They all come in different sizes and shapes. They could be as small as 25 liters, or as large as a 200-liter drum. The best practices are to line these IBCs with plastic poly bags. This is a commonly used practice, although it's not necessarily an industry requirement.

But the point is, if vaccines and medicines can be safely and reliably transported in Intermediate Bulk Containers, they can certainly be stored, transported and delivered in BFS containers made from polymers. Stability testing has been undertaken in more than 50 different products.

When pharmaceutical companies that have a strong portfolio of injectables learn about the benefits of BFS, it opens exciting possibilities. For pharma companies looking for a differentiating factor or a viable alternative to existing formats of primary packaging, BFS might be it.

Blow-Fill-Seal Offers Every Advantage of Prefilled Syringes, and More

With pharma markets in both the West and developing economies rapidly embracing prefilled syringes, the time is right for BFS

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The planned arrival of scalable BFS prefilled injectors (subject to attaining regulatory clearance) is occurring against a backdrop of strong global growth in the prefilled syringes (PFS) market.

According to some research firms, the size of the global PFS market is expected to reach US$22 billion by 2025, at a compound annual growth rate of 11.2%.

We believe the PFS market is growing so strongly because of the increased adoption in economically growing regions such as Asia Pacific, as well as increased adoption in economically established leaders like North America and Europe.

Specifically, the North American market for PFS is estimated to witness a compound annual growth rate more than 10% from now until 2025.

That's mainly due to be increasing prevalence of diabetes and autoimmune diseases which drive industry growth.

In the Asia Pacific region, the prefilled syringe market accounted for approximately $900 million in 2018. It is also expected to witness significant growth in the coming years based on similar factors. For example, India and China both have a large diabetic population, including many cases that remain undiagnosed.

The glass segment accounted for more than 70% of syringe revenue as of 2018. Currently, more than half of the global PFS market is in glass. But regardless of whether they are made of glass or plastic, PFS formats have many advantages.

For home use by patients, PFS support more consistent and longer-term patient adherence to their prescribed health regimens. That’s because they are less trouble to administer, and the patient is assured of getting the right dose assuming it’s a fixed volume rather than a variable dose.

PFS may be a safer and more labor-efficient format than manual filling of traditional syringes, particularly in the clinic or hospital setting. There is less chance of mis-dosing a patient, since the syringe is automatically “precision prefilled” in advance. Also, a great deal of time is saved with the PFS format because the healthcare worker is not required to individually fill each syringe for each injection.

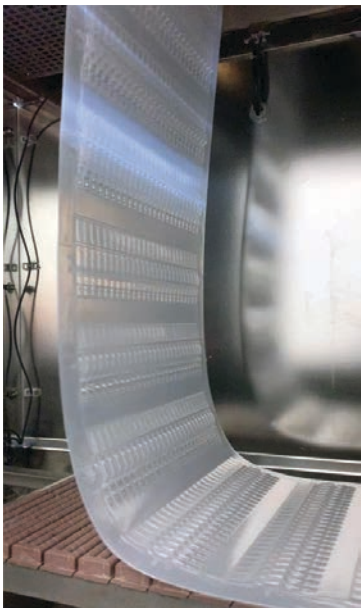
Anecdotally, we have also been advised that a PFS saves time because the administrator never has to wait for the vaccine to settle down and eliminate bubbles in the vial, which sometimes happens.

Again, all of these advantages are present with PFS formats, regardless of whether the vaccine is packaged in glass or plastic. However, there are additional advantages for prefilled syringes that are uniquely associated with using BFS technology.

For example, breakage and delamination issues are very low-risk possibilities with BFS. Pharmaceutical-grade plastic is unlikely to break at non-frozen temperatures and, since it does not have glass, it cannot shed glass particles into the liquid contents.

Scalability can be achieved at accelerated speed for population-wide coverage in a matter of weeks or months, utilizing BFS technology. A single BFS production line can aseptically fill-finish a strip of 25 units every three seconds. Running non-stop, this equates to 25,000 or more units per hour and 720,000 per day, which can total up to 15+ million units per month on a single production line.

Economic efficiency of BFS is very strong, which is a significant factor for a number of Low- and Medium-Income Countries. Equally important is supply chain efficiency. BFS requires only one raw material: pharmaceutical-grade plastic resin. This resin is available in most of the world, with plentiful domestic suppliers in the U.S., and can be stockpiled in a BFS manufacturing facility in



sufficient quantities to produce tens of millions of units – or more -- without requiring replenishment.

(The ApiJect Prefilled Injector also requires a second raw material, which is the stainless-steel rods that become cannula and then needles. Note: The Needle Hub and Connector of ApiJect's Prefilled Injector has been submitted for review but has not been cleared by the FDA or other regulatory authorities.)

Flexibility of design is another key strength for BFS containers. The ApiJect Technology Platform will potentially enable us to meet the specific needs of many pharmaceutical clients, whether it's for a small-volume container (0.5 mL, for which we already have molds) and potentially all the way up to a 50-liter bottle, or perhaps an IV bag. (As noted, above, ApiJect's specific products have not been cleared by regulators.)

Design flexibility also means that BFS can be used to design variations of the Prefilled Injector that could potentially work for lyophilized medicines and for a dual-liquid format. These are on the drawing board now at ApiJect.

But perhaps the most critical strength of BFS is the one identified by the FDA in its 2004 "Guidance" document on this technology. The FDA noted that BFS supports minimal human interaction in the fill-finish process.

Around the world, the era of prefilled syringes is increasingly here. Blow-Fill-Seal looks to be an important part of it.

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