A sponsored Q&A.

Advanced Aseptic Processing

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Weiler Engineering turns raw materials into finished products, such as injectable pharmaceuticals, in one continuous process.

Many products—from medicines to water—need to stay sterile when being packaged. With the ASEP-TECH® Blow/Fill/Seal systems from Weiler Engineering that process can be done quickly and efficiently. Pharmaceutical Technology magazine talked with Andy Goll, Technical Sales Manager for Weiler Engineering, to learn about aseptic liquid processing technology.

Pharmaceutical Technology: What is Blow\Fill\Seal or B\F\S?

Andy Goll: Blow\Fill\Seal is a technology that's actually been around for a little over 50 years now, but it's still considered a new technology for aseptic processing here in the United States. With Blow\Fill\Seal—in kind of a nutshell—you can put raw materials into the machine and you get finished product out. It's obviously quite a bit more complicated that than, but in theory that's the principle of operation.

Pharmaceutical Technology: How does a B\F\S system work?

Andy Goll: You put in the raw materials: the blow molding-grade resin, which is going to form the actual vial or container, and whatever liquid product you would be filling as far as your pharmaceutical drug product. With the system in operation, the resin gets fed into the back of the machine where it's melted under high temperature, and the residence time through the extrusion process is how you're actually forming the sterile container. So as the resin flows through the extruder, it exits the parison head as a molten tube of plastic, which is the interior or the sterile part of the vial.

After the parison is formed, a set of molds will close around the parison, where they will then be transferred under a grade-A filling zone. Underneath the grade-A filling zone, you have positive HEPA filtered pressure air, which is blowing away any potential particles. Then, the filling nozzles will lower into the vial and liquid product—which has been either previously Bulk sterilized or filter sterilized at the point of fill—will then fill into the container. Within a matter of a couple of seconds the nozzles will then raise back into the grade-A environment. The seal molds then close, and that's how you have your finished product.

Pharmaceutical Technology: When you're talking about the system operation how does a B\F\S system actually keep particle generation to a minimum?

Andy Goll: The system itself is really hands-free. So there's very little human intervention, if any at all. Typically, during a B\F\S operation, there are initial start-up steps that would be required by the operators and after that the machine runs itself. It requires zero to very little human intervention—maybe there is a fill-volume adjustment to be made or to clear a jam or something like that. Those are basically the limits to what an operator would be intervening.

The particle generation is at a minimum, especially during the processing of a Blow\Fill\Seal machine for the product itself, mainly because during the parison formation process sterile filtered air blows through that parison. You're creating a positive-pressure environment inside the vial itself with sterile filtered air. So as the mold is closing around the vial you've got sterile air inside the vial, and then as the mold is transferred underneath the grade-A environment you also have HEPA-filtered air in the grade-A environment, which is also being blown around the outside of the vial. So there's no possibility for any ingress of particles into the vials themselves. The combination of just air handling, machine design and no human intervention, that's basically how the system is such a great barrier from any particle contamination.

Pharmaceutical Technology: Why is it that B\F\S is a preferred choice for parenteral manufacturing?

Andy Goll: If you look at B\F\S compared to, let's just say, a conventional glass-filling line, the B\F\S system—like I had said previously—in a matter of seconds is taking raw materials and having finished product all contained in one continuous operation. When you compare it to typical parenteral manufacturing where you're using a glass vial, there are multiple steps involved and, of course, you've got the inventory of your glass vials, the rubber stoppers and the caps. All of that has to be sterilized or cleaned to some level, and then typically you're going to be filling; it could be filled aseptically, but you're also going to be autoclaving. That becomes a problem, especially for heat-sensitive products.

With a Blow\Fill\Seal container you can still autoclave vials if required, but a lot of the companies now—we're finding—are actually looking at this as an advanced process for them, mainly processing heat-sensitive products. You can do low-grade sterilization on some heat-sensitive products, but some products themselves will not tolerate any heat, or heat levels in excess of 40°C has a degradation effect on the active ingredient. With this type of equipment, how you handle the actual product itself through the chilling process and cooling the product down is much easier to handle with a B\F\S container than it would be for a glass vial, which then requires terminal sterilization.

Pharmaceutical Technology: Are there other benefits that are offered to an end-user in comparison to conventional glass production methods.

Andy Goll: The biggest benefit I would say, probably, is its safety. Normally, I think some people would agree that when you have a glass vial where you're actually taking and breaking the glass vial, if you look at that under a high-speed camera you would see the actual shards of glass dissipating during the opening process. With the B\F\S container, of course, that's gone because you're not using glass, and then the types of mold designs offer a whole different set of unique designs, so you can make a multitude of different products on one machine. The flexibility that the Blow\Fill\Seal machine offers is quite enormous with really minimal tooling changes, which adds a huge benefit and the cost to capital remains low as well.

Those are really the main reasons that people are now looking at Blow\Fill\Seal. For one, the safety aspect of getting away from using glass, but you don't require all of these inventoried components. You're not storing the glass vials and the rubber stoppers. With the B\F\S machine, you're basically housing resin and whatever active ingredients you're going to have for the product itself.