→ FORM-FILL-SEAL

INVESTING IN FORM-FILL-SEAL TECHNOLOGY

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Extensive process understanding is required to ensure the consistent manufacture of high-quality sterile parenteral products. At Grifols, our use of state-of-the-art automated aseptic processing systems, including form-fill-seal (FFS) technology, ensures control with minimal human intervention.

WHAT IS FORM-FILL-SEAL TECHNOLOGY?

The form-fill-seal process involves the use of a single piece of equipment to form a plastic container, fill the container with the parenteral drug product and then hermetically seal the container. All of the steps are completed within a few seconds and take place without any operator involvement.

WHY FFS FOR PARENTERALS?

In addition to the pharmaceutical industry, FFS technology is used in food processing and other applications. It is ideally suited for the production of parenteral products; however, because the filling and packaging of the formulated drug product takes place under specific clean room conditions, it is key to minimizing direct human intervention, eliminating contamination risks and thus the possibility of error and maximizing quality assurance and safety.

In general, drug manufacturers want to achieve several fundamental goals, which can include optimizing the cost of drug manufacturing, reducing the lead time for products and ensuring patient safety through the production of the highest quality products – FFS technologies help manufacturers achieve all of these goals for parenteral drug production. With FFS, the container production, filling and sealing processes are all optimized through automation. Lead time is reduced because three discrete steps are combined into one process. In addition, fewer starting materials must be retained in stock, reducing the complexity of managing materials and requiring less storage space.

The products manufactured using FFS technology are inherently safer owing to the automated nature of the process. Elimination of human interaction in the container-forming, filling and sealing processes reduces the risk of contamination or error. In addition, one of the key opportunities for particle generation occurs during the bag molding process. With FFS technology, control over this critical aspect of injectable solution manufacturing is now in the hands of the drug manufacturer.

There are environmental benefits to the process as well: lower energy consumption, reduced waste generation and a lower carbon footprint. Furthermore, the plastic containers do not shatter, like glass bottles and vials, and the resins used to form the plastic containers are recyclable.

MANAGING A COMPLEX PROCESS

FFS is a complex process that combines three steps into one. Establishing an effective manufacturing solution requires extensive understanding of the materials involved and the behavior of plastics. Specialists with knowledge of welding, injection molding, plastic transformation and the incorporation of ports, connectors and other features are needed to design an effective FFS system. Process engineers and machine designers must also be consulted throughout. Completion of a thorough risk analysis is important, and a robust system design based on experience, process data and risk analysis is essential for achieving an efficient, reliable process outcome that generates robust containers and connections that meet all quality requirements.

FFS AT GRIFOLS

Approximately 30 years ago, Grifols moved from glass to plastic packaging materials, and more specifically plastic bags, because of the numerous advantages that they offer. Fifteen years ago, we moved from PVC to PP, and 10 years ago we invested in FFS technology, as we determined that implementing FFS would be the best way to improve the efficiency and ensure the quality of our parenteral manufacturing processes.

In the system implemented at Grifols, the entire process is automated to minimize human manipulation of the product and maximize efficiency. While, for smaller processes, manual loading of the plastic into an FFS system might be prudent, at Grifols we did not want this type of rate-limiting step. Therefore, our FFS system is comprehensive; not only are bag formation, filling and sealing automated, so is the entire process. At the end of the FFS process, the filled and sealed bags are also overwrapped, loaded and unloaded on autoclave trolleys (even loading/unloading of the autoclave is automated) and packaged automatically. As a result, the process begins with plastic film and ends with final product ready for shipment, with inline controls providing real-time monitoring of process parameters and ensuring consistent operation and high product quality. Ultimately, the bags that we produce do not experience human contact until boxes are opened for use in their final hospital destination.

Before we introduced FFS technology into our operations, a thorough risk analysis was conducted, with a plan developed for switching to FFS that would not disrupt timely activity in the plant. Forecasts for product needs and identification of potential roadblocks that could arise were key components of the strategy. Currently, each of our four FFS lines allows the production of 50 million units per year, and we are investing in a fifth line that is expected to receive regulatory approval later in 2019.

LEVERAGING GRIFOLS ENGINEERING EXPERTISE

Development of the FFS system at Grifols involved multiple steps and the contribution of experts within our company, as well as our sister company Grifols Engineering (devoted to the design of pharmaceutical production plants, processes and machinery for both Grifols and other pharmaceutical manufacturers) and machinery suppliers – our goal was to achieve the highest degrees of efficiency and quality in the process.

Thanks to the experience we have acquired over several projects, we have investigated and implemented different types of plastics (e.g., polycarbonate, polypropylene, polyethylene, polyvinyl acetate) throughout our history. Because of this, we have a strong understanding of the plastic's behavior under the conditions present in FFS systems. This information was key to the establishment of appropriate process controls; we also needed to ensure that the FFS system we designed was cleanable and could achieve the needed sterility.

To ensure complete control of the FFS process, we manufacture the components employed in FFS and use equipment developed and manufactured by Grifols Engineering, meaning that Grifols owns the technology. With this vertically integrated approach, Grifols has control of the entire process from start to finish, ensuring that all parts of the manufacturing process are performed following the same high-quality standards.

TAILORED SUPPORT FOR CUSTOMERS

In addition to the general benefits of FFS technology, Grifols customers benefit from the extensive experience we have gained applying this technology for the production of our own products and our control of the entire process. Our experience helps us develop solutions that are optimized for different types of products. Because we manufacture our own bags, we can produce custom bags (i.e., shape, size, composition, types and positions of ports) that meet the specific needs of each customer project and API.

CONTINUED INVESTMENT

The addition of our fifth FFS line will enable Grifols to better meet the needs of our customers going forward. We have been receiving numerous requests for more specialized solutions. The design of the newest line will afford us more flexibility to produce products with a wider variety of bag design options. In addition to this type of significant investment, we are continuously expanding our knowledge of the FFS process and identifying ways to enhance its robustness and increase the safety of the process and our products. We are very proud to be able to offer form-fill-seal technology to our customers and help them efficiently produce high-quality products. P

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Lluc Mercadé joined the Grifols group in early 2016, with over 20 years of experience behind him. Lluc has worked in chemicals and cosmetics, in addition to the pharmaceutical industry. He has developed his career mainly in engineering, maintenance and production, and has also worked as a professor at the Universidad Politecnica de Catalunya. Lluc currently serves as the Manufacturing Director at a Laboratorios Grifols plant, devoted to the manufacturing of intravenous products.

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