Overcoming the Pitfalls of Pre-filled Syringe Filling

Michael Isele, Site Manager at Recipharm, explores the pitfalls of filling and packaging in pre-filled syringe formats, from sterile integrity requirements, to packaging challenges, such as kitting, explaining how these challenges can be addressed.

The international pre-filled syringe market was worth $3.6 billion in 2021, and is predicted to increase in value to $6.5 billion by 2030, growing at a CAGR of 7.1% throughout the forecast period.[1]

One of the key drivers for this projected growth has been a major change in the choice of injectable delivery formats following the COVID-19 pandemic.

Governments and pharmaceutical companies worked together to deliver an unprecedented global mass vaccination programme to protect patients from potentially fatal coronavirus symptoms. To deliver this, the pharmaceutical industry focused on developing effective vaccines in a short timeframe, usually filled into vials.

While this approach was successful in achieving its goals, areas for further improvement were flagged, particularly when it came to maximising the number of people vaccinated every day. Every time a patient arrived for their injection, a syringe had to be prepared and filled from a vial. The cumulative impact of the time spent carrying out this process for each appointment was significant, restricting the number of vaccinations that could take place each day.

For future outbreaks, it is important to identify ways of allowing doses to be administered quickly and efficiently to maximise the number of people vaccinated per day. Pre-filled syringes offered an ideal way of achieving this goal, as they arrive ready-prepared with the required dosage inside, streamlining the preparation process for each individual administration.

Following the success of pre-filled syringes in the COVID-19 vaccination programme, there has been a significant increase in interest from pharmaceutical companies in pre-filled syringes for future vaccine applications, such as influenza vaccines. Companies are also considering them for biologic therapies to treat chronic conditions, such as cancer and autoimmune diseases, which are driving growth in the parenterals segment overall. This is because the nature of biologics means that most treatments have to be delivered by injection. They are also being considered as a potential solution to allow tourists planning to visit countries where malaria and other diseases are endemic to self-administer their vaccines instead of seeing their doctor.

The Quest for Useability and Patient Centricity

Useability and patient experience are significant challenges for many drug developers across all dosage forms, but for injectable drugs in particular. Providing patients with the ability to self-administer their treatment, without the need for support from a healthcare provider (HCP) or carer, can enhance convenience for the patient. Moreover, it can free up professionals' time, reducing strain on the limited resources of many national healthcare services still recovering from the effects of the COVID-19 pandemic.

Enhanced convenience can significantly enhance patient adherence to their treatment which, in turn, can have a positive impact on the effectiveness of therapy. In doing so, it can further relieve pressure on healthcare systems by minimising the need for patients with chronic conditions to be seen by doctors.

Traditionally, injectable dosage forms have had a key disadvantage when it comes to useability and self-administration compared with rival forms, due to the complexity of preparing standard syringes for administration. For older patients in particular, dexterity issues, poor eyesight and other age-related conditions all add to existing useability challenges inherent to injectables. This can exacerbate many patients' existing reluctance to take injectable treatments, due to negative perceptions about needles, which can further impact on patient adherence.

With this in mind, a growing number of pharmaceutical companies are exploring options to make injectable drug products easier for patients to use themselves in a non-clinical setting, such as their home, or school or workspace.

Pre-filled syringes are one crucial way of achieving this goal for drug products that need to be delivered by injection. As they come already charged with the precise amount of drug formulation for a single dose, they enable patients to self-administer, without the need to precisely measure out their dose beforehand. This minimises the risk of over- or under-dosing, while streamlining complex preparation requirements, saving patients a considerable amount of time and stress.

As such, pre-filled syringes offer considerable potential for pharmaceutical companies looking to support patients with more patient-centric therapies, across a range of applications and conditions, including vaccines.

Nevertheless, while pre-filled syringes offer a number of benefits, they do pose challenges for pharmaceutical companies, particularly when it comes to filling and packaging them efficiently and in accordance with stringent regulatory requirements. Failure to address these challenges could have an impact on the success of the finished product.

The Pitfalls of Pre-filled Syringe Production

Manufacturing and filling pre-filled syringes can be a complex process compared with other dosage forms. There are a number of considerations that companies should be aware of:

- **Sterile fill and finish are crucial** – All parenteral dosage forms must be processed and packaged in a sterile and contained environment, and pre-filled syringes are no exception. This is crucial to ensure optimum hygiene and safeguard patients' health, and to maintain compliance with stringent regulations, such as the European Union's (EU) Annex 1. With this in mind, it is vital to have access to cleanroom facilities, with production lines featuring restricted access barrier systems (RABs) and/or other advanced

aseptic processing controls. These can be expensive for pharmaceutical companies to install and operate on their own, particularly if they are only needed for a single drug product. It can also be challenging to secure and maintain large-volume sterile filling capacity for large-batch projects, such as a multinational vaccine roll-out.

- **Employee safety and cross-contamination protocols need to be in place –** If the drug product contains a biological active or a highly potent active pharmaceutical ingredient (HPAPI), then additional containment protocols need to be in place to manage any toxicity risks. Having good spill responses in force can protect line operatives in the event of a breakage and safeguard against cross-contamination of other products.

- **Unique packaging issues need to be considered –** the packaging of pre-filled syringes can present specific issues for manufacturers. Not only are the needles fragile, requiring careful handling and robust secondary packaging solutions, they also often come in syringe kits accompanied by a number of components – more so than for other dosage forms – which can complicate the packaging process itself. In addition to the standard label and plunger rod, a pre-filled syringe may be packaged with a loose or stake needle, as well as a safety device, which may feature a finger flange or a backstop. Alcohol pads may also be included for sterilising the skin prior to injection, or information leaflets in the secondary packaging to offer guidance on using the syringe for patients.

- **Cold-chain transit may be required –** As we saw in the early stages of the COVID-19 vaccine roll-out, some mRNA vaccines and biologic treatments have unique temperature requirements that need to be adhered to during transport and storage. Some vaccines need to be stored and shipped at -70°C before being brought up to room temperature just before administration. Ensuring these environmental controls throughout the entire journey of a parenteral drug – whether in pre-filled syringe form, or otherwise – can be a particular challenge, especially when shipping to emerging economies, which may not have the cryogenic infrastructure in place.

- **Labelling is crucial –** If pre-filled syringe products are destined for multiple markets, then extra consideration needs to be given to product labelling. Labels need to comply with all of the relevant local regulations for each target market. They must also be written in the relevant local languages to ensure that patients can read and understand them.

- **Traceability is key –** More and more, regulatory authorities around the world require pharmaceutical companies to explore how to trace their pre-filled syringe and other products as they move from the production line to reach patients in order to prevent counterfeit products entering the supply chain.

Meeting these needs can be difficult for manufacturers to achieve, especially when producing pre-filled syringe products for the first time.

Addressing the Challenges

To overcome the challenges of producing pre-filled syringes and meet growing demand for more patient-centric injectables, more and more pharmaceutical companies are outsourcing their pre-filled syringe processing to contract development and manufacturing organisations (CDMOs).

Advanced CDMOs with a strong track record of filling pre-filled syringes and other injectable formats are well placed to provide pharmaceutical companies with the support they need to commercialise their pre-filled syringe drug products. They will already have the dedicated sterile filling infrastructure in place, as well as the manufacturing, regulatory and other expertise to support in manufacturing pre-filled syringe products. As such, they can eliminate the need for pharma companies to invest time and resources into building new lines to produce their product.

Some CDMOs invested in large-volume sterile filling capacity at the height of the COVID-19 crisis, featuring the latest flexible equipment, to support the pharma industry in delivering billions of vaccine doses for global distribution. These partners are ideally positioned to support pharma companies developing large-batch injectable treatments, including vaccines for seasonal boosters or future pandemics.

CDMOs are constantly evolving their sterile fill and finish offering for injectables to enhance the support they offer pharmaceutical companies as they respond

to changing demand from patients and HCPs. As such, they can be an ideal partner to support companies seeking to harness the benefits of pre-filled syringes to deliver a better experience for patients.

Looking Ahead

The potential of pre-filled syringes to enable the more efficient delivery of mass treatment campaigns and allow more flexible administration of treatments for chronic diseases outweigh the challenges of filling them. As such, we can expect the market to continue to grow and diversify for the foreseeable future.

Working with an expert with the sterile manufacturing and filling capacity customised for pre-filled syringes can overcome challenges and ensure pre-filled syringe products are manufactured, filled, and delivered safely and efficiently.

REFERENCES

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