INTERVIEW

In this interview, Piyush Agarwal of Tjoapack talks with ONdrugDelivery about the current state of the injectable pharmaceuticals market and how working with a specialist contract packaging organisation can help pharma companies navigate their product through this rapidly evolving sector and deliver their product to market on time.

PIYUSH AGARWAL, TECHNICAL SOLUTIONS & SUPPLIER MANAGER, TJOAPACK

Piyush Agarwal heads Technical Solutions and Supplier Management at Tjoapack. He has been with Tjoapack since early 2019 and has executed multiple functions, including business development and project implementation. His team is responsible for finding operationally feasible and commercially viable solutions for pharmaceutical companies to pack their products on time. He is also responsible both for managing contracts and negotiations with existing suppliers and for onboarding new suppliers. He holds a Bachelor's degree in Engineering and a Master's in Business Administration.

Q To begin, let's discuss the major trends, aside from patient-centricity, in the prefilled syringe (PFS) and injection sphere. First, are there any new devices or innovations in syringe design that are becoming more popular among pharmaceutical companies?

A The demand for PFSs has been steadily increasing over the past decade. Alongside this, other injectable devices that improve the injectable medicine administration experience have been developed in tandem. For instance, autoinjectors, injection pens and infusion pumps have also been actively increasing their share in the sterile manufacturing market.

As for syringe components, engineers are actively exploring integrated safety systems that can be applied to the PFSs. These tend to focus extensively on needle safety, usability and multi-barrel options. Specialists are actively expanding syringe portfolio ranges with respect to product volume options and needle sizes.

Q In your opinion, what is the current position of PFSs in the pharmaceutical space?

A PFSs have become the primary alternative to multi-vial solutions when it comes to biologics and biosimilars. On the current market, PFSs are extensively used for antithrombotics, vaccines, biologics and small molecules. The use of PFSs in these areas helps to improve the manufacturing process, avoid waste and ensure that the correct dose is administered.

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The current pharma market has seen a significant shift towards therapeutic segments like immunology, oncology and gene therapy. As such, biologics are now being given a higher priority in the pharmaceutical industry's pipeline. The administration of biologics is mostly performed via injection, as alternative routes of administration often drastically lower their effectiveness.

Within biologics, monoclonal antibodies (mAbs) have the largest market share, followed by vaccines and insulin. For small-molecule injectables, the leading segments are oncology and anti-infectives. mABs accounted for one quarter of the total revenue share in biologics in 2019, primarily due to the expanding product pipeline and a high rate of approvals by the US FDA and EMA. Additionally, according to the recent filings, the most prominent growth areas are oncology and immunology.

In general, a large and diverse group of manufacturers are investing in the development and commercialisation of biosimilars. This, in turn, is facilitating the demand for new packaging solutions for injectables. When we look at the current pharmaceutical pipeline and, in particular, clinical and preclinical trials, small molecule and mAB therapies are dominant. Additionally, we're also seeing the preferred delivery route change along with this shift in pipeline priorities. There is a decrease in the oral delivery route, while the injectable route increases.

Q Do you expect upcoming new regulations to impact the use of PFSs?

A Currently, supportive government regulations, such as needlestick legislation, are providing a boost to PFS market growth. This legislation promotes the widespread implementation of PFSs with integrated safety systems to reduce the rate of needlestick injuries.

Additionally, the recent Institute for Safe Medication Practices (ISMP) guidelines heavily support an increased use of ready-to-administer (RTA) syringes. The ISMP guidelines have increased awareness and guidance regarding the use and manufacture of RTA syringes. In their guidelines published in 2020, the ISMP once again addressed the main downsides of admixing faced by clinicians during emergency situations, introducing new safe practices that include the use of RTA products. Similar guidelines are also being released by other regulatory bodies and serve as an additional driver for the PFS market.

Q Can you tell us about any new approaches to the packaging of PFSs and other injectable devices?

A As PFSs and other devices become more sophisticated, their packaging needs have shifted from solely carton-based packaging to a more stable and durable packaging solution. While carton-based packaging does offer some form of structural stability with the inclusion of paper-based custom inlays to keep the devices in place, there are alternate approaches to packaging injectable devices in cartons. Two such approaches are placing them in an unsealed blister with a clamp-in option and a sealed blister with or without a clamp-in option.

These trends are leading companies to adopt various non-standardised solutions. Forward-thinking contract packaging organisations (CPOs) are addressing these needs by investing in secondary packaging capabilities so that they can be flexible in order to meet market requirements. The services such companies can offer range from manual customised package assembly to automated packaging of PFSs into blisters.

Advanced blistering lines can automate the secondary packing of injectables, including vials, ampules and PFSs, into rigid PVC with high thermoformability. These PVC blisters are then sealed, ensuring that all components remain intact. The blister, along with a patient information leaflet, is then placed inside a carton that can be serialised later or aggregated based on market-specific requirements.

Q How does a CPO manage the transfer of the product from the contract manufacturer or the pharmaceutical company to its facility for packaging PFSs?

A First, the quality and integrity of the product needs to be ensured. The key considerations for this are analytical tests (performed by certified third parties at the client's wish); identifying key components (safety device and format parts for plunger rods, backstops or finger flanges); identification of necessary packaging materials (such as foils and films) with subsequent stability studies executed by a certified third party; and quality validation to ensure that each step of the PFS assembly process is safe for the end-product and patients to use.

The packaging of PFSs differs from the packaging of other dosage forms, such as oral solids and vials (Box 1). Oral solids are primarily packed into blisters, bottles and similar, and therefore have different in-process controls to ensure that there is no contamination. Since oral solids come in different sizes and shapes, there is not always one standard solution that fits all. However, for PFS packaging, the key

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BOX 1: PACKAGING PROCESSES STEP-BY-STEP

PFSs
- Manual infeed of syringes
- Plunger rod insertion station
  - Infeed of plunger rods
  - Sorting of plunger rods
  - Plunger rod insertion
  - Syringe rotation with adjustable speed and torque to allow fine adjustment
- Labelling
  - Labelling is done via a separate unwinding unit
  - Labelling is synchronised with the rotation speed of the syringes
- Label printing
  - Label printing is done via thermal transfer to include variable data
- Safety device station (optional)
  - Infeed of safety device
  - Pick-up and pushdown of device
  - Finger flange assembly station
- Backstop assembly station
  - Infeed of backstops
  - Sorting
  - Assembly
- Blistering
  - Thermoforming pockets for placing PFSs
  - Feeding PFSs, vials and/or needles into pockets
  - Lidding and sealing
- Carton unit
  - Placing sealed blister into the carton with a leaflet
- Serialisation unit
- Automated case packer
  - Placing cartons into shipper
  - Optional aggregation
- Tertiary packaging.

ORAL SOLIDS (BLISTERING)
- Bulk feeding
- Blistering
  - Thermoforming pockets for placing tablets
  - Lidding and sealing
- Carton unit
  - Placing sealed blister into the carton with a leaflet
- Serialisation
- Tertiary packaging.

ORAL SOLIDS (BOTTLING)
- Bulk feeding
- Bottling
  - Tablet counting
  - Bottle feeding
  - Induction sealing (if applicable)
  - Adding silica gel (if applicable)
  - Adding space filler (if applicable)
  - Capping (snap-on or twist-off)
- Carton unit (if applicable)
  - Placing sealed blister into the carton with a leaflet
- Serialisation
- Tertiary packaging.

VIALS (SECONDARY PACKAGING)
- Manual infeed of vials
- Labelling
- Label printing
  - This is done via thermal transfer to include variable data
- Inlay station
  - Adding an inlay for single or multi-vial packs (optional)
- Carton unit
  - Placing inlay or single vials into the carton with a patient information leaflet
- Serialisation unit
- Tertiary packaging.

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considerations are the type of PFS assembly (with or without a safety device) and format parts for plunger rods, backstops or finger flanges. Identifying the optimum foil with deep stretch properties to hold the PFS in its blister and a suitable lidding foil are some of the other key considerations.

Q How can a CPO support its customers in managing these issues?

A An established CPO can leverage its own experience, along with that of its suppliers, to create a tailor-made solution for its customers. It's also important to include a dedicated project and technical team in the production team to ensure that all the equipment is correctly installed and that operators are sufficiently trained with the equipment. It is also prudent for the CPO to provide a management team dedicated to finding technically feasible and commercially viable solutions for clients that help them meet their requirements, as well as a dedicated project management and implementation team to ensure that products are delivered to the patient on time.

Q What is the best way for pharmaceutical companies to address the unique challenges they face when packaging their products?

A When it comes to packaging, the current challenges faced by pharmaceutical companies include securing key components for format parts and/or equipment and key packaging materials for secondary and tertiary packaging, as well as having the agility to ensure that new products are launched to new markets on time and the flexibility to adapt to different regulatory, market, equipment and process requirements. To meet these challenges, it is key to have a packaging partner that can support with scalability from clinical trial to product launch to commercial high-volume batches.

Q What are the challenges facing pharmaceutical companies when ensuring the traceability of their products?

A Nowadays, the serialisation process is well-established and implemented within all key markets. However, challenges still arise from the differences in serialisation requirements across different markets, such as Europe, the US, India, China and Russia. For example, while serialisation within Europe is uniform (except for Italy and Greece), many companies come across difficulties when they decide to go international. The differences are concentrated around medicine verification systems, the extent of required "Track & Trace", pick processes for different markets and mandatory aggregation.

Q Could you explain the challenges of the labelling process for treatments?

A Different markets have different language requirements, which makes stock-keeping unit artwork management critical. There is also the consideration that some markets, such as Switzerland and the Benelux countries, have multiple language requirements, which leads to more complex booklets and labels. Lastly, it's critical to realise that the varying temperature requirements of products makes choice of label and adhesive material crucial.

Q How can CPOs overcome the challenges of labelling in cold and ultra-cold environments?

A Standard labelling process are often done under ambient conditions in the range of 15–25°C. However, for cold-chain products (2–8°C), it is prudent to follow the product guides of "Time Out of Range" to ensure that the end-product temperature conditions are met. Optimum label materials should selected to ensure proper adhesiveness even under condensation. For ultra-cold environments (-20°C), one solution is to label and pack products on dry-ice trays.

ABOUT THE COMPANY

Tjoapack is a global CPO specialising in primary and secondary pharmaceutical packaging and supply chain management services. The company is dedicated to shaping the future of the pharmaceutical supply chain to be safer and more reliable for its customers and for patients. With a track record of almost 30 years in contract packaging, Tjoapack uses its knowledge and experience to offer flexible solutions to its customers' challenges and uses the latest technologies to improve its operations continuously. The company now supplies products to over 40 countries across all continents.

Tjoapack

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