DEVICE MANUFACTURING FROM DEVELOPMENT THROUGH COMMERCIALISATION

In this article, Sheleagh Dougan, Business Development Manager, and Meredith Canty, Director Drug Delivery Systems, both of SMC Ltd., give an overview of the scales of manufacturing throughout the design of a new combination product and the necessary considerations at each one.

This article is based on an SMC Ltd. white paper: "Insights Into Drug Delivery Device Manufacturing From Development Through Commercialization".

INTRODUCTION

Over the past decade, the pharmaceutical industry has witnessed the emergence of biologics and targeted therapies, resulting in abundant opportunities for pharma companies. With technological advancements and a greater understanding of effective treatment options, novel delivery methods are being introduced, giving pharma companies a competitive edge and offering patients better solutions for their needs.

For drug delivery device engineers, this opens up opportunities to design innovative device solutions that meet both the needs of these new formulations and their target patient demographics. Prefilled syringes remain a viable option for applications administered by healthcare professionals. Patients who self-inject are faced with various challenges, often due to the very disease they are managing, such as limited joint mobility from rheumatoid arthritis, vision limitations from migraines or the stress of administration in an emergency situation. As such, sophisticated patient-centric devices are being introduced and embraced.

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In the past, pharma has viewed the drug delivery device as a secondary concern. This way of thinking is easy to understand since many drug delivery devices are, by definition, secondary packaging. This approach often left little-to-no time to develop the optimal drug delivery solution for the patient. Device engineers were forced to use existing technologies to meet the established timelines, which in turn resulted in less-than-ideal device solutions. Pharma has since recognised this as an issue and is changing to include device teams in early stages of drug development. This allows the team appropriate time to design and develop an optimal delivery method to meet the needs of the patient as well as the needs of the formulation.

When developing a combination product, a greater opportunity for success exists when the device technology is optimised to meet the patient and stakeholder needs. When those needs cannot be met with an existing platform, selecting a knowledgeable team with the design, development, regulatory and manufacturing knowledge to meet the requirements results in a robust device design with greater chance of successfully launching in the market.

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Manufacturing Finished Devices From Concept To Completion

Product Development

- Design for Manufacturability (DFM)
- Risk management and FMEA
- Develop pilot manufacturing
- Producting testing development
- Supplier sourcing and qualification
- Manufacture devices for:
  - Engineering testing
  - Human factors studies
  - Usability testing
  - Design verification testing

Clinical Trial Manufacturing

- Manufacture clinical trial devices
- Process validation (IQ/OQ/PQ)
- Regulatory documentation support
- Commercialisation planning
- Supply chain management
- Finalise:
  - Product specifications
  - Functional testing
  - Design freeze
  - Packaging and Labeling

Commercial Manufacturing

- FDA pre-approval inspection
- Manufacture launch quantities
- Regulatory approval
- Customer product release review
- Product life cycle management
- Scalable manufacturing:
  - Launch with pilot solution
  - Increase capacity to forecast
  - Implement semi-auto solution
  - Implement fully-auto solution

Figure 1: Considerations at each scale of manufacturing prior to product launch.

The capabilities needed to evolve a drug delivery device from product development through commercial manufacturing are shown in Figure 1. Whether pharma companies outsource some or all of these phases, the device team must plan accordingly for product development, clinical trial manufacturing and commercial manufacturing. An overview of each of these phases follows.

PRODUCT DEVELOPMENT

During formulation development, the pharma company will determine the best device path forward with either a novel device technology or a modification to an existing device platform. Whether the device team is located within the pharmaceutical company or contracted to a product development consultancy, it is important to engage the device manufacturing partner at this stage. This ensures that the device is optimised for manufacturability at the projected commercial product volumes within the expected bounds for timeline, device quality and financial requirements.

The device manufacturing partner should provide significant input on the device design. Analysing the device from the tooling, moulding, assembly, automation and testing perspectives, ensures that the design and manufacturing methods are robust for long-term manufacturing. The manufacturer should also provide the pharmaceutical company with scale-up plans for the device, including the risks and benefits associated with each phase of the product lifecycle. Part of this process includes understanding the device specifications and reviewing the design failure mode effects analysis (dFMEA). Understanding what is critical from a design perspective allows the device manufacturer to create manufacturing solutions that de-risk the manufacturing process.

The device manufacturing partner should propose the best path forward from a tooling and assembly perspective. The manufacturer should initiate a process failure mode effects analysis (pFMEA) to identify and prevent as many risks as possible. The pFMEA should be reviewed by both the manufacturer and the pharma company to ensure all parties understand the areas of risk. If there are areas that have too much risk, a review will determine possible solutions to reduce it. Identifying risks early allows for the planning of risk mitigation solutions to create balance between risk, cost and timeline. The device manufacturing partner should utilise these analyses to fabricate pilot tooling and equipment to manufacture devices for product testing development, human factors studies, design verification testing, stability testing and other requirements for development.

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CLINICAL TRIAL MANUFACTURING

Prior to obtaining regulatory approval for a combination product, several phases of clinical trials must be performed to collect the requisite safety and efficacy data. Due to the high cost of clinical trials and the length of time to complete all phases, it is critical to have high quality, fully-functional devices available for the clinical trial. This can be achieved by partnering with a device manufacturer that has the necessary quality systems, including US FDA 21 CFR Part 4 compliance. Being Part 4 compliant allows the device manufacturer to handle and integrate the drug product, then perform the final combination product assembly, labelling and packaging. By utilising a single source to manufacture the combination product, a pharma company can reduce risk and cost, and put their focus on preparing and executing the clinical trials.

Clinical trial manufacturing should be discussed during the product development phase. The device manufacturer should provide a robust solution to develop a device that is capable of meeting clinical trial low-volume, high-quality requirements. When reviewing the pFMEA, it must be considered that the device could be for human use at this phase, therefore risks must

be mitigated and controls must be in place. Examples of risk mitigation controls are proper pack-out configuration of components or implementing 100% inspection of a critical specification during assembly.

COMMERCIAL MANUFACTURING

It is important to start planning for commercialisation as the combination product advances through each clinical trial phase to ensure the device is as robust as possible, risks have been properly mitigated and a manufacturing plan has been put in place to ensure that the tools and automation can achieve the projected volumes. Depending on the commercial manufacturing solution, the timeline to develop, design, build, test and validate new tools and automation can exceed a year. The timeline and budget must be discussed early in the programme to ensure all parties agree on a commercial manufacturing path and the point in time at which the plan will be initiated.

A critical decision for combination products is the location for manufacturing, labelling and packaging. If the decision is to outsource this activity to the device manufacturing partner, all preparations for the FDA pre-approval inspection must be initiated as early as possible. All quality systems must be appropriately updated, validation activities made robust and an internal audit conducted to review and address any gaps prior to the FDA audit.

Another critical component is the launch strategy. When developing a commercial launch strategy there are multiple factors to consider including device specifications, projected annual volumes, timeline, capital budget and target selling price. Launching the product as soon as practical after regulatory approval provides both market and financial benefits. This ideal situation can be achieved by launching with the validated pilot tools, equipment and processes utilised for engineering and clinical manufacturing. A thorough pFMEA should be conducted and reviewed together with the pharma company so that all parties understand the benefits and risks associated with launching with this strategy. Although the capacity of the initial manufacturing line may not meet the needs for future product growth, the device contract manufacturer can utilise the knowledge gained during the device development and plan ahead to provide manufacturing options to meet the quality, forecasted volume and economic targets throughout the lifecycle of the product.

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SUMMARY

Biologics and other targeted therapies often require low annual volumes, however the device manufacturing strategy must still fit commercial expectations. Optimal manufacturing solutions should be identified to meet the quality, financial, timeline and patient needs of the product.

Including the device manufacturing partner as an early member of the device team provides important input to ensure that the device is designed for long-term robust manufacturing, risks to the product and processes have been mitigated and that a phased approach manufacturing plan is used. A launch strategy that takes into account the device specifications, projected annual volumes, timeline, capital budget and target selling price ensures the pharmaceutical company's targets are achieved and the device launches successfully. Finding the right manufacturing partner greatly improves the likelihood of this success.

ABOUT THE COMPANY

SMC Ltd. provides contract manufacturing of single-use devices for the healthcare, pharmaceutical and diagnostics industries. Dedicated to medical manufacturing, SMC provides full product services from initial concept through final packaged device including: programme management, design and development, product manufacturing, clinical manufacturing, electronics integration and global supply chain management.

ABOUT THE AUTHORS

Sheleagh Dougan, Business Development Manager, SMC Ltd., has over 20 years of experience in the healthcare manufacturing industry. She has worked on the development and commercialisation of life-saving combination products in both programme management and business development roles. Currently, Ms Dougan is leading the effort of developing new business opportunities in the drug delivery market through new and existing customer relationships.

Meredith Canty, Director of Drug Delivery Systems, SMC Ltd., has over 20 years of experience in the drug delivery space from a contract manufacturing perspective. Ms Canty has worked with many pharmaceutical companies, design firms and manufacturers to launch new drug delivery devices. Her experience ranges from managing the launch of new drug delivery combination products to increasing capacity on an existing product line by more than 50 million devices per year.

DRUG DELIVERY DEVICE MANUFACTURING

SMC provides global contract manufacturing solutions of single-use devices for the pharmaceutical, medical and diagnostics industries with full product services from initial concept through final packaged device. To see how we can partner with you on your next device visit: www.smcltd.com

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