ROUNDTABLE REPORT

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Specialty Medicines: Keys to the Packaging Process from the Clinic to Commercial Launch

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KEY TAKEAWAYS

- To mitigate risk, pharmaceutical and biopharmaceutical companies should consider commercial packaging decisions far earlier in the clinical process.
- Pharmaceutical and biopharmaceutical companies irrespective of size can benefit from working with an experienced, specialist packaging partner.
- Many companies find it beneficial to partner with a single packaging vendor from the early stages of development through to commercial launch.
- Within pharmaceutical and biopharmaceutical companies, it is beneficial for the clinical and commercial teams to work collaboratively during the early phases of development and not in silos dictated by phase.
- Technology-forward packaging can prevent counterfeiting, maintain product safety, and promote patient adherence.
- In response to the COVID-19 pandemic, aspects of both the clinical and commercial processes are evolving, challenging the historical norm.

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OVERVIEW

During the product development process, clinical teams in pharmaceutical and biopharmaceutical companies often defer commercialization-related decisions, including those associated with packaging. As regulatory mandates, product delivery systems, and supply chains become more complex, earlier focus on commercial packaging considerations may reduce risk and lead to both time and cost efficiencies. Both large and small companies have found that by partnering with a third-party packaging vendor with specialist expertise, they are able to better manage the hurdles associated with regulatory approvals and global product launches, and confidently manage unexpected obstacles. This has been particularly evident given the current global coronavirus pandemic, whereby expert packaging vendors have been able to navigate and deliver time-critical clinical and commercial packaging solutions including complex Cold Chain requirements for both treatment and vaccination programs.

CONTEXT

A panel of experts from across the pharmaceutical and biopharmaceutical industry discussed key aspects of the clinical to commercial paradigm and best practices when managing the end-to-end packaging process. This included the importance of applying packaging design principles and ensuring launch packaging considerations were included at each stage of the development life cycle in order to deliver a successful, time-efficient launch.

KEY TAKEAWAYS

To mitigate risk, pharmaceutical and biopharmaceutical companies should consider commercial packaging decisions far earlier in the clinical process.

When pharmaceutical and biopharmaceutical companies engage in new product development, there is a historical tendency to focus on the immediate needs of the clinical phase. As a result, many commercialization-related decisions—including packaging— are deferred, which may lead to increased risk as well as missed opportunities to expedite launch, reduce overall cost, and ultimately drive earlier commercialization and speed to market.

In terms of industry best practices for example, Astellas generally initiates detailed discussions relating to commercial product attributes when products achieve the clinical proof of concept milestone, though the timing of this discussion can be earlier if required based on the development timelines for the product. The goal is to prevent the CMC (Chemistry Manufacturing and Controls) dependent activities required for registration from potential time additive further product development.

New and innovative products such as biologics and vaccines have led to increased complexity of the product delivery systems and the regulatory and environmental landscape, which in turn has led to an increase in the breadth of commercial packaging considerations. The panelists shared several reasons why pharmaceutical companies must think about packaging earlier.

- **Complicated delivery systems and supply chain requirements.** In the biotech space, for example, some products have Cold Chain and ultra-Cold Chain requirements. In addition, the ever-evolving area of drug delivery systems often immediately trigger the need for more sophisticated packaging. For example, patient centricity is key when dealing with self-administration of products delivered through vials, pre-filled syringes, and autoinjectors. The packaging of these medicines, particularly when thinking about the scale-up for commercial launch, may require a technology-forward and often bespoke packaging solutions. For example, some autoinjectors now include wraparound devices aimed at improving dexterity and grip of the patient.

- **Serialization.** A requirement in the United States under the Drug Supply Chain Security Act (DSCSA) and in the EU under the Falsified Medicines Directive (FMD). In the event that products flow through a specialty pharmacy, opportunities exist to carry forward end-to-end track and trace functionality to the patient as the end user.
- **The regulatory pathway.** If products are on fast track or have breakthrough therapy designation, clinical development is greatly accelerated, and CMC development can become rate limiting to submission. In such situations, early decision making related to CMC is required.
- **Unexpected FDA requirements.** The FDA may insert unanticipated demands into its review processes. Before DSCSA was enacted, Carl Accettura worked with a company on an implantable controlled substance. The FDA required the company to serialize kits in order for doctors to securely record the authenticated kits received. This became a part of the risk evaluation and mitigation strategies.
- **Non-oral combination products.** Complexity increases exponentially when dealing with non-oral combination products. For example, companies must evaluate how sterilization procedures interact with packaging for injectables and implantables. Although teams may have optimized the sterilization method for the drug product, they may not have considered the impact on packaging and therefore packaging requirements.
- **Human factors.** Traditionally, with delivery forms such as inhalers, companies have had to demonstrate the human factors associated with administration of the product. These requirements are creeping into injectables and even now to solid oral dose and powders. The FDA, as an example, expects companies to proactively demonstrate that they have thought through human factors. It is becoming a game changer in packaging development.
- **Green credentials and carbon footprint issues.** Green credentials and strategies aimed at reducing carbon footprint are key considerations. However, many companies do not consider such factors during the development cycle and it is only when trying to enter specific markets that potential risks to commercialization present; for example, the Nordics where use of PVC is frowned upon.

> The global regulatory landscape for combination products and Serialization are rapidly evolving. The interaction between sponsors and packagers is important because you need flexibility to respond to a changing environment.
>
> *John DeMay, Astellas*

Pharmaceutical and biopharmaceutical companies irrespective of size can benefit from working with an experienced, specialist packaging partner.

Due to internal resource constraints, many smaller pharmaceutical and biopharmaceutical companies rely on consultants and outsourcing partners for their packaging requirements. Often, larger companies will also consider partnering with a packaging specialist for a variety of reasons which may include internal capacity or capability constraints particularly when entering new markets. It is of critical importance that any packaging design partner is familiar with the actual manufacturing and packaging technologies as these can have a dramatic impact on the packaging process itself. Utilizing a pure design partner with no link to the packaging process can lead to both cost and time challenges.

The panelists discussed three criteria they consider when selecting a packaging designer or partner:

1. **The ability to create prototypes during the clinical process.** The FDA is increasingly interested in how companies present drug packaging. Some have been asked to present in advance, the kit packaging that they plan to use at launch. It has also been found that using prototypes during patient and physician focus groups can be extremely beneficial as part of the packaging design process, yielding true insight into patient usability and acceptability.

> A picture is worth a thousand words and a prototype is worth a million. Developing prototypes during the clinical process is invaluable.
>
> *Carl Accettura, PharmoRx Therapeutics*

2. **Organizational culture.** Softer considerations such as the partner's quality culture and collaboration framework are seen as being important. A truly collaborative relationship between the sponsor and packaging partner is critical when reacting to unexpected developments that arise during the clinical stages. Astellas, for example, looks at the strength of the partner's project management group and its ability to collaborate and solve problems during the project life cycle.
3. **Engineering capability.** Even if a company has an in-house packaging engineering function, it is still seen as beneficial to work with a partner that works with multiple companies at a global level, as this experience provides the ability to offer a different perspective, share best practices and help teams think outside the box. This additional experience has been proven to help differentiate products within the marketplace and make drugs more acceptable to patients.

> When we are focused on all the technical details of product development from drug substance synthesis to finished drug product manufacture and testing under accelerated timelines, it's good to have a packaging partner who will add value by engaging with us on packaging issues. For instance, how can we balance the need to have clinical packaging meet the child protection requirements of the US CPSC while ensuring it has minimal impact on the ease of use for the patient population in the clinical study?
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> *Arul Joseph, Avanir Pharmaceuticals*

Many companies find it beneficial to partner with a single packaging vendor from the early stages of development through to commercial launch.

Working with a partner able to bridge seamlessly from the early stages of clinical development through to commercial launch can be far simpler than using one partner during the clinical phases and then switching to another for commercialization. Packaging partners with an international presence for both clinical and commercial needs are a great option for pharmaceutical companies planning global launches.

Some companies adopt a multi-regional facility strategy for packaging, meaning they are able to respond to the unique needs of particular regions or markets. Regional requirements are the norm within the EU, where member countries have different mandates relating to Serialization, Braille, child-resistant packaging, and more. Even in the United States, some states expect the prescribing pharmacy to ensure that tamper-evident seals are placed on units going to patients. Having a single partner able to both understand and accommodate a multi-regional packaging approach is clearly an advantage for pharmaceutical companies.

When selecting a packaging vendor, it is important to evaluate whether the clinical and commercial divisions are synergistic, open, and communicative. Pharmaceutical and biopharmaceutical companies may want to inquire whether the clinical and commercial divisions work from a central set of design standards for example. This approach results in the best product innovation, while minimizing risk and time to market.

Within pharmaceutical and biopharmaceutical companies, it is beneficial for the clinical and commercial teams to work collaboratively during the early phases of development and not in silos dictated by phase.

In the past, the handoff between clinical and commercial groups could be described as a relay race, however, the industry has evolved over time and now recognizes that clinical and commercial teams need to interact strongly with each another. Today, best practice would see commercial teams engage with clinical during the earlier stages of development and post launch, development teams be involved for at least the first year or two, especially for complex products.

It should be noted that this collaborative way of working sometimes breaks down, for example, when an overseas parent drives the clinical and regulatory aspects and a newly formed commercial team based elsewhere is responsible for launch. Although the commercial team is the right party to contract for commercial packaging, the overseas parent holds the NDA. In this situation, teams must consider what SOPs need to be in place and what dialogue needs to occur.

> In a large pharma, the clinical team may not even know who the commercial team is and vice versa. At small companies, people wear multiple hats and may be in both camps. If we're doing our part well with strong project management, we prompt them to engage in dialog and drive to some of the decision points.
>
> *Justin Schroeder, PCI Pharma Services*

Technology-forward packaging can prevent counterfeiting, maintain product safety, and promote patient adherence.

As the complexity and price of therapies increase, counterfeiting is also bound to increase. To combat this problem, pharmaceutical companies may want to move beyond radio-frequency identification (RFID) to individual unit-level technologies. Another area for consideration is smart packaging that monitors patient adherence as studies have shown that over 50% of patients in clinical trials do not adhere to their dosing regimens.

Opportunities may exist to leverage the DSCSA 2D barcode mandate to track and trace products through to the patient. If patients have an application on a GPS-enabled smartphone, pharmaceutical

companies could provide them with additional product information and prompts which would be particularly valuable for specialty medications. Another technology-forward idea is to integrate temperature monitoring with authentication.

In response to the COVID-19 pandemic, aspects of both the clinical and commercial processes are evolving, challenging the historical norm.

COVID-19 has affected many aspects of pharmaceutical product development. Regulatory audits of facilities in the United States and overseas ground to a halt, with some agencies now conducting virtual audits and FDA guidance expected in the coming weeks about the use of livestreaming video.

From a packaging perspective, many companies are moving to virtual audits of packaging partners. Many are also evaluating whether their packaging and transportation designs are robust enough to navigate the points in the supply chain where adjustments have been made.

Not surprisingly, the pandemic has affected pharmaceutical distribution. If caregivers or patients are unable to get to the clinical site, companies are considering whether site-to-patient or direct-to-patient distribution are viable options. Until now, ideas such as decentralized clinical trials were purely a theoretical concept. Today, they are a necessity.

BIOGRAPHIES

Carl J. Accettura
Vice President and General Manager, PharmoRx Therapeutics

Carl Accettura has over 35 years of Biopharma industry experience, starting in Big Pharma, with Merck, Pfizer, Roche, and BMS. In 1997, Carl entered emergent, virtual Pharma company life and he never looked back. Carl built CDMO-driven supply chain networks at Anesta, Cephalon, RxKinetix, Kyowa Hakko Pharmaceuticals, Dainippon Sumitomo Pharma America, Sunovion Pharma, Braeburn Pharmaceuticals, FORUM Pharmaceuticals, PharmoRx Therapeutics, and Nobelpharma Anmerica. Carl's current focus is on novel Rare Disease & CNS pharmaceutical product development and commercial readiness, with emphasis on innovation in cold chain logistics and novel Specialty Pharmacy supply chain, market access, and dispensing models. Carl earned a B.S. with distinction from Cornell University in Mechanical Engineering. He holds a M.S. from University of Illinois and a M.B.A from the Stern School at New York University

John DeMay
President, Astellas US Technologies and Executive Director, Project and Product Management, Astellas

John is a leader with nearly 34 years of pharmaceutical industry experience in a variety of roles related to product development, manufacturing technology transfer and R&D administration. Since 2017, John has served as President of Astellas US Technologies, Inc. and Executive Director, Project and Product Management. In these roles, he is responsible for coordination of CMC (Chemistry, Manufacturing and Controls) development and manufacturing/supply activities for multiple products and for the smooth collaboration of multiple US-based functions in two corporate divisions: Pharmaceutical Technology (the CMC/Manufacturing division) and GMP (Good Manufacturing Practice) Quality Assurance.

Arul Joseph

Senior Director, Pharmaceutical Development and Clinical Supply, Avanir Pharmaceuticals

Arul Joseph leads the Pharmaceutical Development and Clinical Supply Chain function at Avanir Pharmaceuticals. He has about 15 years of experience in chemistry, manufacturing, and controls (CMC) and has held roles of increasing responsibility at Gilead Sciences, Merck, and Schering Plough. Before joining the pharmaceutical industry, he conducted postdoctoral research at the Scripps Research Institute in La Jolla, CA. Arul earned his PhD in Organic Chemistry from the University of Maryland in College Park, MD, and an MBA in Strategy and Finance from New York University's Stern School of Business in New York, NY.

Justin Schroeder

Vice President, Global Program Management, PCI Pharma Services

Justin Schroeder is the Global Vice President of Product Development and Commercialization at PCI Pharma Services. Mr. Schroeder is responsible for ensuring PCI's global clients realize seamless lifecycle management and successful commercialization of their therapies. With more than 20 years of experience in outsourced pharmaceutical services in various roles including Package Engineering and Design Development, Project Management, Marketing and Business Development, in his current role he leads various functional disciplines in the creation and application of innovation solutions for clients across the development lifecycle, ensuring consistent execution of PCI's #1 Commitment to provide the industry leading customer experience.

Paul Smallman

Director, Technical Operations, PCI Pharma Services

Paul has over 25 years' experience in pharmaceutical packaging design, development, operations and New Product Introduction, fulfilling customer requirement, both known and unknown. Managing in excess of 50 launches a year for various size pharmaceutical companies. Customers drawing upon Paul's expertise guarantees them regulatory compliance and cost effective, innovative solutions.

Akriti Seth (Moderator)

Senior Reporter, Pharma Intelligence

As a correspondent for Channel NewsAsia, Singapore and for India Technology News, Akriti has covered a wide range of subject-matter including politics, economics and technology for a B2B audience. She has also gained experience working for Bloomberg TV India and Mid-Day Mumbai. Akriti is a graduate of the University of Mumbai and holds a masters from Mumbai's Xavier Institute of Communications. Most recently she has worked as a freelance journalist in London, where she is now based, having lived there for the past two years. She enjoys photography and blogging.