TATA CONSULTANCY SERVICES

Building on belief

The urgent need for a combination product adoption strategy

Abstract

The **combination product** market has witnessed significant growth with the recent scientific and technological advancements. Any combination of drugs, devices and biologics are considered combination products, a few examples are inhaler, nasal spray, transdermal system or a drug or biologic with an administration device like auto-injector or prefilled syringe. Market analysts anticipate that the combination product industry will grow to $186.7 billion by 2027, expanding at a CAGR of 6.4%.[1]

There are numerous benefits of combination products; for example, reduction of drug waste (e.g., prefilled syringes provide the right amount of drug dose, compared to the additional 20-30% amount in vials), reduced cost of drugs (where manufacturing cost of drugs are high), avoidance of exposure to toxic products when delivered through separated vial and needle, and so on. All these benefits have been surely a blessing to the patients. Previously, cancer patients had to visit clinics after chemotherapy to take a specific drug; now, it is administrated through an auto-injector at home. Additionally, self-administration has been instrumental as telemedicine has been widely accepted by users amid the COVID-19 pandemic.

However, there is always another side of the story; the conveniences of the combination products may create unforeseen complexities if the development and manufacturing of its constituents are disjointed.

The need for cohesiveness

Traditionally, pharmaceutical and biotechnology companies' processes and adherence to regulatory compliance requirements have been drug and biologic-focused, while the processes of design, development, and manufacturing of the administration devices were considered separately. One of the reasons for not having an established process with these companies is a lack of regulation until few years back. For example, the Current Good Manufacturing Practice Guidance (cGMP) for combination products 21 CFR Part 4 had not evolved until 2013[2].

Now, companies have realized the need to define an integrated and cohesive process and adhere to compliance of drug or biologic and device design, development, and manufacturing of their combination products. There have been instances where regulatory authorities like the US Food and Drug Administration (FDA) have provided their observations and warning letters to the pharma and biotech companies alleging that they have not met the proper standards of resources and controls in the production processes.

The strategy for accelerating combination product adoption

While the need for cohesiveness is recognized and regulatory guidelines (e.g., 21 CFR Part 4 cGMP for combination products) are in place, it is still difficult to define and implement end-to-end processes in the value chain, starting from combination product design to commercialization.

Before defining and implementing the processes, the challenge is to change the legacy of isolation and the mindset of people in the organization. Industry leaders need to break from the tradition and guide the bio-pharma companies to act like medical device companies and drive comprehensive strategies for

[1] iHealthcareAnalyst, Inc., accessed August 24, 2021, https://www.ihealthcareanalyst.com/global-drug-device-combination-products-market/

[2] govinfo, Code of Federal Regulations, accessed August 25, 2021, https://www.govinfo.gov/content/pkg/CFR-2013-title21-vol1/pdf/CFR-2013-title21-vol1-part4.pdf

combination products. To build an integrated working environment, both departments must understand each other's common objectives, processes, sciences, and technologies.

The leadership team must enable cross-training for each group. The drug or biologics development team needs to understand device development factors like design control, human-centric usability design, etc. The device development team needs to understand drug or biologics development factors such as scale-up, process transfer, etc.

On the execution side, companies must develop new strategies and processes with deep knowledge of both the worlds of bio-pharma and medical devices while complying with individual guidelines for a device (e.g., 21 CFR Part 820), and drug (e.g., 21 CFR Part 210 and 211).

Advancing combination product development:

One way to get combination products to market faster is to build an integrated clinical strategy for drugs and devices. If the device design and development team understand the drug or biologic clinical phases, they can plan the scale of device manufacturing to ramp up drug development. While clinical and commercial production requires adhering to cGMP, the prototype does not require it.

Integrating science and engineering of the drug or biologic and device is critical for success. For example, the material used for the biologic's auto-injector may impact drug efficacy; this may delay the overall combination product launch if developers don't engineer the product cohesively.

The overall risk management of drug or biologics and devices, including the quality target product profile (QTTP), needs to be integrated for all possible scenarios. It is advisable to initiate the device design through CAD models, drawings, parts, attributes, failure modes and effects analysis, and bill of materials (BOM); and regulatory deliverables including design history file (DHF) and device master record (DMR), and device specifications at the same time and in collaboration with the processes of drug substance development.

The integration of the product and its lifecycle management requires an integrated system too. The objective is to build and maintain the final combination of product information cohesively during the development and manufacturing cycles.

Navigating regulatory challenges across countries:

Before developing a combination product, creators must determine the product's regulatory agency and associated compliance requirements. These regulations will vary based on the product's country of origin.

For example, the US has multiple departments within the FDA regarding the regulations for drugs, devices, and combination products, including:

- The Center for Drug Evaluation and Research (CDER) - for products like inhalers
- The Center for Devices and Radiological Health (CDRH) - for products like drug-eluting stents
- The Center for Biologics Evaluation and Research (CBER) - for products like syringes prefilled with cellular therapeutics

Determining which center to register a product with, in the US, depends on the primary mode of action (PMOA), which identifies the combination products single most important therapeutic area being treated by the product. If US-based developers struggle to determine PMOA, they can submit a pre-request for designation (Pre-RFD) and a request for designation (RFD) to the FDA's Office of Combination Products (OCP).

Companies with specific competencies need to review their processes and establish a suitable set of compliance processes to receive approval for marketing, manufacturing practices (cGMP), and post-market safety. Each individual part of the combination product must be compliant with the constituent's regulatory agency.

Cognitive platform critical for safety reporting:

There is a critical need to adopt an integrated process for combination product safety surveillance and reporting. A cognitive automation-based platform for combination product safety management—covering end-to-end process automation from complaints intake to processing, process improvement and finally reporting to regulatory agencies—is the critical step towards conducting post-market safety reporting (PMSR). The platform requires the capability to differentiate automatically between reactions to the drug or device, process the complaint through the appropriate module, and produce an integrated safety report.

The way forward

With the technological advancements and the rise of telemedicine amid the COVID-19 pandemic, the need of the hour is to enable and promote a combination product that benefits patients. It is time to re-consider and implement a fresh strategy and process for combination product design, development and manufacturing.

The story does not end here—it is the beginning of the journey for harmonization. It's time for companies to come together to build a strategy to integrate global (or regional) regulations like Medical Devices Single Audit Plan (MDSAP) and European Medical Device Regulation (MDR) in the combination product context.

In the rising demand for personalized medicine, the combination product development and manufacturing processes need end-to-end agility, to provide better care to patients.

This is a call for companies to strategize their journey of combination products for faster, cost-optimized, and compliant development, and manufacturing of their products. Through full strategic integration, we can revolutionize the combination product market.

About the authors

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Harminder is a business segment head and leads TCS' US West and Mid-West Life Sciences Unit, primarily responsible for Biotech and Medical Devices segment. He has been with TCS for over 23 years and has held various roles with increasing responsibility. He has a rich experience in P&L management, consultative sales, account / relationship management, outsourcing, delivery, and pre-sales. He has worked across multiple geographies with Life Sciences customers. Harminder is a passionate leader with high focus on customer-centricity and helping customers achieve their strategic objectives and business outcomes with the power of digital technologies. He enjoys building, nurturing, and working with diverse global teams.

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Ranga is a client partner for TCS' US West and Mid-West Life Sciences Unit and leads multiple customer relationships, and portfolios of its biotech and medical device customers. He has 21 years of experience in Information Technology and Business Process Services with Sales and Delivery responsibilities, including 14 years in the medical devices and bio-pharma industries. He has partnered with his customer to delivery many transformative programs in Financial Planning & Analysis (FP&A), Data and Analytics, Manufacturing, IT Service Management (ITSM) and Service Desk etc., globally. He has helped many organizations to adopt Cloud, Agile and DevOps (people, process, and technologies) early in the industry. He holds a Bachelor's degree in Computer Science and Engineering with multiple professional credentials from Project Management Institute, The Open Group and Scrum Alliance.

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