

Navigating the Complexities of Advanced Therapeutic Medicinal Products: The Critical Role of Specialized CDMOs

The landscape of pharmaceutical development is rapidly evolving, with advanced therapeutic medicinal products (ATMPs), which include gene therapies, cell therapies, and tissue-engineered products, at the forefront of this transformation.

As of April 2023, a total of 25 ATMPs were granted marketing authorization in the EU¹. In the United States, there are currently 34 FDA-approved cell or gene therapies². The development pipeline for ATMPs is robust, with over 2,200 clinical trials being conducted globally, including 216 in Phase III³. This indicates a significant number of ATMPs are on the horizon, poised to transform the therapeutic landscape.

These innovative therapies offer unprecedented potential for treating a range of diseases, many of which were previously deemed untreatable. However, the journey from development to patient delivery is fraught with complexities, particularly in the realms of labeling, packaging and distribution.

This article delves into the intricacies of working with ATMPs and underscores the benefits of outsourcing these critical tasks to an experienced Contract Development

and Manufacturing Organization (CDMO) with innovative processes, facilities and highly specialized, skilled teams.

The Unique Challenges of ATMPs

ATMPs are fundamentally different from traditional pharmaceuticals. Their complexity arises from their biological nature, the need for precise handling, and stringent regulatory requirements. These factors collectively make the labeling, packaging and distributing of ATMPs a highly intricate process.

Unlike small molecule drugs, ATMPs are derived from living cells and tissues. This biological basis introduces variability and sensitivity that must be meticulously managed. For instance, gene therapies often involve viral vectors that require specific storage conditions to maintain stability and efficacy. Similarly, cell therapies necessitate a controlled environment to preserve cell viability. Any deviation from these conditions can compromise the product's integrity, making precise handling and processing essential.

In addition, the regulatory landscape for ATMPs is stringent and continually evolving. Regulatory bodies such as the FDA and EMA have established

rigorous guidelines to ensure the safety and efficacy of these therapies. Compliance with these regulations requires a deep understanding of the specific requirements for each type of ATMP. Labeling must accurately reflect the product's identity, potency, and storage conditions, while packaging must ensure protection from environmental factors and contamination whilst always maintaining the required temperature.

ATMPs often require specialized handling and storage conditions. For example, many cell therapies must be stored at ultra-low temperatures (-20 thru -80°C) to maintain cell viability. This necessitates the use of innovative packaging solutions that can withstand extreme conditions. Additionally, the handling process must be carefully controlled to prevent contamination and ensure the product's integrity. These requirements add layers of complexity to the labeling, packaging and distribution process.

The Intricacies of Labeling, packaging and distributing ATMPs

Given the unique challenges associated with ATMPs, the labeling, packaging and distribution process must be meticulously planned and executed. Certain products may be so specialised e.g. one vial per batch, necessitating rapid turnaround and QP release for direct patient distribution within 24-48 hours. This involves several critical steps, each of which

requires specialized knowledge and expertise.

Customization and Flexibility


One of the primary challenges in labeling and packaging ATMPs is the need for customization and flexibility. Unlike traditional pharmaceuticals, which often have standardized packaging solutions, ATMPs require bespoke solutions tailored to their specific characteristics. This includes custom labels that provide detailed information about the product, such as its genetic composition, storage conditions, and expiration date. Additionally, packaging solutions must be flexible enough to accommodate different types of ATMPs, including vials and syringes.

Traceability and Serialization

Traceability is a critical aspect of ATMP handling. Given the high value and sensitivity of these products, it is essential to have robust systems in place to track and trace each product throughout the supply chain. This involves the use of serialization techniques, such as unique barcodes or QR codes, that enable real-time tracking and verification. These systems not only ensure product integrity but also facilitate compliance with regulatory requirements.

Quality Control and Assurance

Quality control and assurance are paramount in the management of ATMPs. Each step of the process must be carefully monitored and validated to ensure compliance with regulatory



standards and product specifications. This includes rigorous testing of packaging materials to ensure they provide adequate protection and stability. Additionally, given the ultra low temperature environment, the use of appropriate labels must be considered to ensure stickability is not compromised and printed text remains legible. Any inconsistencies can have serious implications for patient safety and product efficacy.

The Benefits of Outsourcing to a Specialized CDMO

Given the complexities and challenges associated with ATMP labeling, packaging and distribution, many pharmaceutical companies choose to outsource these tasks to specialized CDMOs. An experienced CDMO offers several key benefits that can significantly enhance the efficiency and effectiveness of the entire process.

Expertise and Experience

One of the primary advantages of outsourcing to a specialized CDMO is access to expertise and experience. CDMOs have dedicated teams of professionals with extensive knowledge of ATMPs and the specific requirements for their intricate handling. This expertise ensures that all regulatory requirements are met and that the products are handled with the utmost care and precision. Additionally, CDMOs have experience working with a wide range of ATMPs, enabling them to develop customized solutions tailored to each product's unique characteristics.

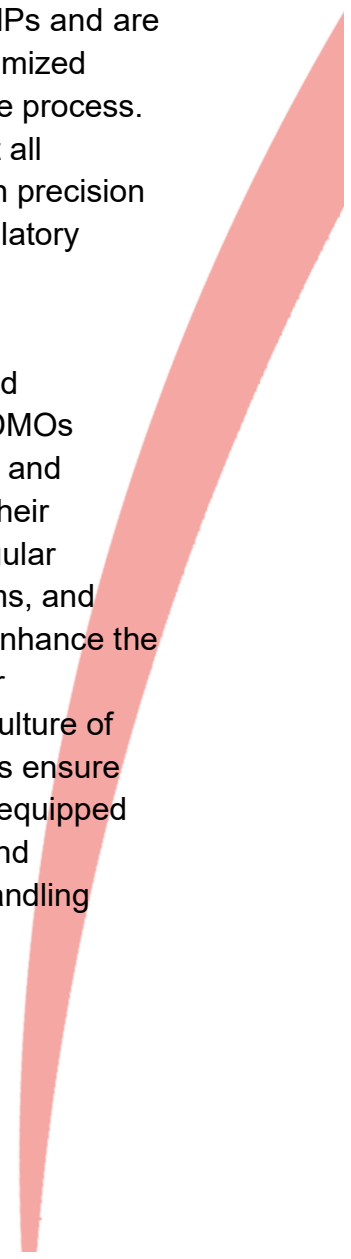
Experienced Teams and Highly Trained Workforce

The success of a CDMO in handling the complexities of ATMPs largely depends on the expertise and experience of its workforce. Here are some key aspects that highlight the importance of having experienced teams and a highly trained workforce:

Specialized Knowledge and Skills

CDMOs invest significantly in ensuring their skilled employees are kept up to date on the latest innovative techniques to ensure the handling and processing of these sensitive products. These experts are well-versed in the unique requirements of ATMPs and are capable of developing customized solutions for each step of the process. Their expertise ensures that all activities are carried out with precision and in compliance with regulatory standards.

To stay abreast of the latest advancements in ATMPs and regulatory requirements, CDMOs invest in continuous training and development programs for their workforce. This includes regular workshops, training programs, and certification programs that enhance the skills and knowledge of their employees. By fostering a culture of continuous learning, CDMOs ensure that their teams are always equipped with the latest information and techniques necessary for handling ATMPs.



Cross-Functional Collaboration

Effective labeling and packaging of ATMPs require close collaboration between various departments, including quality control, quality assurance, engineering, logistics and project management. CDMOs foster a collaborative environment where cross-functional teams work together seamlessly to address the unique challenges of ATMPs. This collaborative approach ensures that all aspects of the process are aligned and optimized for efficiency and compliance and most importantly guarantees timely delivery of the final product to the patient in need – this can be as low as 20 hours.

Attention to Detail

Given the high stakes involved in ATMPs, attention to detail is crucial. Experienced teams at CDMOs are trained to meticulously follow protocols and standard operating procedures (SOPs) to ensure that every step of the labeling and packaging process is executed flawlessly. This attention to detail helps prevent errors that could compromise product integrity or patient safety.

Problem-Solving Capabilities

The dynamic nature of ATMPs often presents unforeseen challenges that require quick and effective problem-solving. Highly trained teams at CDMOs are adept at identifying potential issues and implementing solutions promptly. Their ability to troubleshoot and resolve problems efficiently is essential for maintaining


the quality and integrity of ATMPs. Effective and continuous communication with the client is crucial to enable smooth management from the very outset of the project.

Advanced Technologies and Facilities

Specialized CDMOs invest in advanced technologies and state-of-the-art facilities to support the labeling and packaging of these highly specialized treatments. This includes sophisticated serialization and traceability systems, as well as specialized packaging solutions designed to maintain product stability and integrity. These technologies enable CDMOs to provide high-quality, reliable services that meet the stringent requirements of regulatory bodies and ensure the safety and efficacy of the products.

CDMOs, like Almac Pharma Services, have invested significantly in their dedicated Ultra-Low Temperature (ULT) solutions in Europe and the US enabling operations to be conducted at temperatures ranging from -20°C to -80°C. These facilities, innovative equipment and highly skilled teams combined with just-in-time labeling, packaging, and serialization to meet the specific requirements of each product offers a completely tailored approach for each individual product and client.

Innovative shippers, temperature monitors, and digital platforms are used throughout every stage of the process to provide real-time visibility



into the conditions of the product. Should the required temperature range be compromised at any stage, the monitors will trigger an alert and procedures will be implemented with immediate effect to handle in the most effective and efficient way.

Scalability and Flexibility

Outsourcing to a specialized CDMO also offers scalability and flexibility. CDMOs have the capacity and resources to handle large volumes of products and can quickly scale up or down based on demand. This flexibility is particularly important for ATMPs, which often require rapid turnaround times and the ability to adapt to changing requirements. Additionally, CDMOs can provide customized solutions that accommodate different types of ATMPs and their specific labeling, packaging and distribution needs.

Cost-Effectiveness

Outsourcing labeling, packaging and distribution to a specialized CDMO can also be cost-effective. By leveraging the expertise, technologies, and facilities of a CDMO, pharmaceutical companies can reduce the costs associated with in-house processing. This includes savings on equipment, materials, and personnel, as well as the potential for reduced regulatory compliance costs. Additionally, outsourcing allows companies to focus on their core competencies, such as research and development, while leaving the complex tasks of labeling,

packaging and distribution to the experienced supplier.

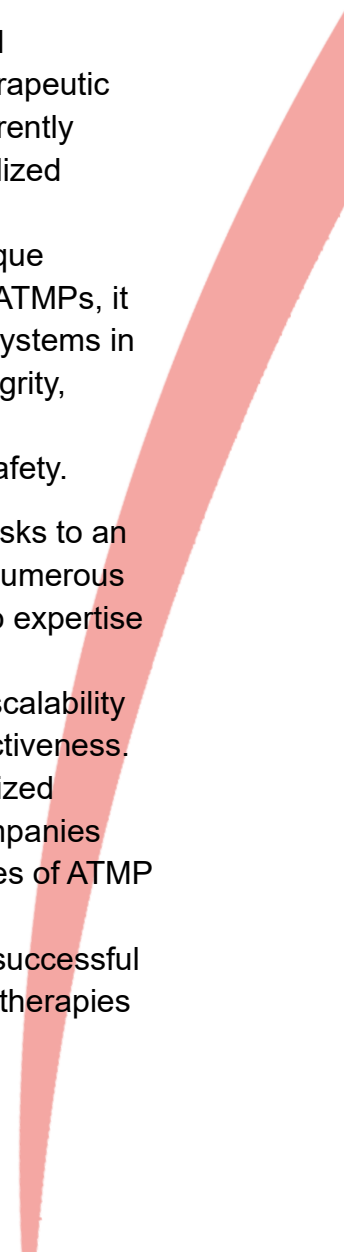
Regulatory Expertise

Navigating the complex regulatory landscape for ATMPs requires in-depth knowledge and experience. CDMOs employ regulatory experts who stay up to date with the latest guidelines and requirements from regulatory bodies such as the FDA and EMA. These experts ensure that all activities comply with regulatory standards, thereby facilitating smooth approval processes and market access for ATMPs.

Conclusion

The labeling, packaging and distribution of advanced therapeutic medicinal products are inherently complex and require specialized knowledge, expertise, and technologies. Given the unique challenges associated with ATMPs, it is essential to have robust systems in place to ensure product integrity, compliance with regulatory requirements, and patient safety.

Outsourcing these critical tasks to an experienced CDMO offers numerous benefits, including access to expertise and experience, advanced technologies and facilities, scalability and flexibility, and cost-effectiveness. By partnering with a specialized CDMO, pharmaceutical companies can navigate the complexities of ATMP labeling and packaging with confidence and ensure the successful delivery of these innovative therapies to patients in need.



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