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Clinical Supply CDMOs Rejig Service Models

CGTs and DTP trials supercharge bespoke solutions demand.

Momentum is picking up aggressively across the clinical supply services providers to reconfigure their offerings as next-gen biotherapeutics and direct-to-patient (DTP) trials transform the clinical research arena disrupting the traditional supply models.

The rapid surge in advanced biopharmaceuticals is fueling a burgeoning trial sector with a requirement for specialized clinical supplies solutions tailored for biologics and cell and gene therapies (CGTs).

"The increased opportunity afforded by next-generation biotherapeutics brings with it increased clinical supply chain complexity and risk," said Lyn McNeill, supply chain solutions manager, Almac Clinical Services, a global contract development and manufacturing organization (CDMO) based in Northern Ireland.

If vital components of the supply chain—technology, packaging and labeling design, and production strategy—are approached retrospectively or in silos, risks and inefficiencies result, alerts McNeill. This in turn will make responding quickly and effectively to sudden, unforeseen disruption infinitely more challenging.

Working steadfastly on re-configuration over the years,

Almac has established services in place to cater to the full scale of supply chain needs across the CDMO's customer portfolio of over 600 pharma and biotech companies worldwide.

To capitalize on the potential offered by CGTs, ensuring the right drug is delivered to the right patient at the right time and within specification, Almac works in close partnership with its clients by promoting early and frequent planning, incorporating flexibility into delivery, and maintaining supply viability.

McNeill drives home the point that the ability to flex and manage change at every stage of the CGT development lifecycle is not only important, but also critical.

Further, to ensure the integrity and viability of precious CGT products Almac offers a comprehensive range of digital supply chain services which share data points in real-time and coordinate with multiple trial stakeholders, including Interactive Response Technology (IRT) and clinical sites.

ENSURING AN UNBROKEN CHAIN

Breakthrough therapeutic products come with inevitable associated challenges such as the requirement of increasingly complex handling requirements.

For cold chain handling, Almac has recently launched a cryogenic service solution from the company's Durham, NC, facility. With a capacity for more than 40,000 vials -150 to -196 and a validated cryo shipping service, the CDMO says it can ensure an unbroken chain of custody from the product line to the patient for advanced CGT trials.

Lean manufacturing, just-in-time labeling and just-in-time manufacturing in addition to personalized clinical packaging and labeling solutions, which utilize specialist materials designed to cater to the precise needs of CGT, are among Almac's service offerings to CGT trial sponsors to help overcome the challenges of low-yield, high-value products and unpredictable recruitment.

In line with Almac, many clinical supply CDMOs are rapidly expanding their capabilities such as cold chain handling and packaging solutions to support increased demand for the distribution of biologic drugs and CGTs as these advanced therapeutics are slated to grow at a much higher pace. (*Also see "New Modalities Hog the Limelight" - Contract Pharma, May 2023*).

Catalent, which has been bolstering its clinical supply solutions for advanced therapeutics through a series of expansion activities for the last couple of years, provides an example.

A global leader in clinical supply services, Catalent added storage, kitting, and distribution of advanced therapies at ultra-low temperatures (ULT) for clinical trials at its facility in Shiga, Japan in May 2023 besides completing a $2.2 million expansion to its clinical supply facility in Singapore last February. The latter involved the installation of an additional 35 new freezers for ULT storage to handle biopharmaceuticals and advanced modalities, including mRNA-based vaccines, and CGTs.

A month ago in the same year, Catalent announced the launch of its new Case Management Service for supply chain oversight for advanced therapy medicinal products from program start to finish. Earlier, in December 2022, the CDMO completed the expansion of its clinical supply facility in the Waigaoqiao Free Trade Zone (FTZ) in Shanghai, China to include clinical supply management, comparator sourcing, demand-led supply, primary and secondary packaging, storage, and global distribution, as well as clinical returns and destruction.

ON-DEMAND LABELING

The innovative, non-traditional clinical supply solutions are seen far more striking in packaging and labeling services.

"In addition to small batch/quick-turn packaging, we are seeing an increase in cryogenic packaging and smart labels," said Leslie Gurland, vice president of sales and marketing at Premium Label & Packaging Solutions (PLPS). She also maintains that the globalization of medicine has led to the desire for additional booklet pages to accommodate more languages.

With a wealth of expertise as an innovator in labeling and packing solutions for 45 years, PLPS can support both large and small applications. The U.S.-based firm produces a full range of clinical trial labels, including booklet labels up to 60 pages, multiple wrap labels, single-ply labels, 2-ply peel reseal labels and labels with removable secondary labels attached.

Personalized medicine/advanced therapy medicinal products caused the need for greater flexibility to support customized short production runs, which has driven printers to look at equipment and processes that support the quality and cycle time customers need.

Working in a digital environment to process art files, issue PDF proofs, produce in-house plates, and use automated equipment to 100% inspect finished print copy are now standard requirements, Gurland noted.

DEMAND-LED SUPPLY

"Modern trials are increasingly intricate, encompassing diverse locations, intricate protocols, and specialized requirements," said Sanjay Vyas, executive vice president, safety and logistics, and country head of India at Parexel, one of the world's largest contract research organizations (CROs) providing the full range of phase I to IV clinical development services. Managing this complexity in-house can be demanding, prompting companies to leverage the expertise and resources of dedicated providers, he adds referring to the increasing clinical supplies outsourcing activity.

Parexel opened a clinical trial supplies and logistics depot in Suzhou, China in September 2022 equipped with capabilities including temperature storage (-20°C, 2-8°C, 15-25°C, -80°C), secondary packaging and labeling, fulfillment and distribution, and drug sourcing for biopharma customers.

Even as advanced personalized/precision therapy products make clinical studies more and more complex, the rising preference for decentralized, direct-to-patient trials post-COVID-19 warrants a radical remodeling of clinical supply chains.

Reports show that nearly a quarter of clinical studies now offer a home-based solution.

This accelerated shift to decentralized clinical trials (DCTs)/direct-to-patient trials (DTPs) has brought clinical drug supply functions to become more central to the investigator and patient experience. It has necessitated tailored packaging design, last-mile delivery and returns, patient-device support services, trial-data management, and user interfaces for investigators.

In addition, there is a primary emphasis on the customization of clinical trial supply solutions—mainly for personalized medicine and precision therapies—aligned with patient profiles.

Per program requirements, for example, the amount of clinical trial material for personalized therapeutic products like CGTs has now been greatly reduced, unlike traditional models. This often requires CDMOs to have the right-size facility and equipment for smaller batch sizes.

Finding that DTP distribution options can be advantageous to sponsors, many CDMOs are now offering DTP services alongside comprehensive clinical supply solutions.

Demand-led supply and direct-to-patient distribution services launched by Catalent, for example, are intended to allow for more streamlined processes and patient-centric studies through enabling on-demand GMP secondary packaging, labeling and distribution of patient kits based on actual patient need rather than relying upon large static inventories.

DIRECT-TO-PATIENT—LAST MILE DELIVERY

Direct-to-patient supply services, according to clinical supply experts, reduce the burden of patients to visit clinical sites and maintain participation.

DCTs, Vyas says, offer advantages such as reduced barriers to participation, greater inclusion of diverse populations, and improved efficiency in recruiting and retaining patients, despite certain challenges related to drug transportation, storage, and security.

In addition to focusing on sending clinical supplies straight to patients' homes, Parexel employs advanced technology and operational excellence principles to ensure accurate supply forecasts, sophisticated reporting, and consolidation of purchasing, storage, assembly, and transportation processes in DTP trials.

Kelly Corkey, director, clinical supplies management, IRT, ICON, also shares the view that adopting a DTP model increases enrollment and accessibility to medicines, especially for people in low- and middle-income countries (LMICs). This, coupled with a home healthcare solution, can support increasing medication adherence.

However, Corkey cautions that since this is an emerging model, not every site will have experience with DTP or DCT models. A lack of DTP and DCT-specific training may be a frustration felt on the site side.

ICON, a global CRO headquartered in Dublin, Ireland, offers tailored supply chain solutions across therapeutic areas with capabilities to conduct temperature excursion adjudication in-house and support CGTs in several capacities, including scheduling apheresis manufacturing and generating the cell handling manual.

ICON's clinical supplies project managers work closely with the IRT team to peer review the clinical supplies modules ensuring that the customers receive the best end-user experience.

"Our focus as clinical supplies experts is getting the right drug to the right place, at the right time. Whether that is at a patient's home or a clinical trial site, we apply the same set of GMP and GCP standards to documentation and processes," said Corkey.

HYBRID MODELS TO RISK-PROOF SUPPLIES

However, considering the complex and ever-changing environments of clinical trials, many CDMOs employ strategies combining both traditional and innovative supply approaches to create an agile and flexible supply system that can swiftly respond to changes.

"While we recognize the propelled growth of the CGT and personalized/precision medicine market, we believe that traditional approaches to clinical supply do also have their place," said McNeill.

As such, Almac offers four cornerstones of packaging options: traditional, lean, just-in-time labeling and just-in-time manufacturing.

The challenge, according to McNeill, is balancing multiple demand channels with uncertain volumes and limited supply and then choosing the correct strategy to meet the clinical need.

Expert teams at Almac provide direction in relation to hybrid models which combine traditional and innovative approaches within the same study and even at the same time.

For example, at the beginning of a CGT study, when supply demand is unpredictable and the geographical locations of the patient population unclear, just in time manufacturing could be adopted to carefully conserve the valuable supply. Once enrollment has stabilized, the switch can be made to a more traditional approach. The tipping point requires planning and early communication to ensure process alignment and smooth transition down the line, McNeill concludes. **CP**

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