From lab to patient: efficient cold chain management for advanced therapy trials

In light of the mounting complexities associated with cutting-edge cell and gene therapies and the growing demands of cold-chain logistics, how can clinical trial supply chains progress and meet these evolving challenges effectively?

Gunter Van Hoof at Clinigen

Ensuring successful cold chain handling of investigational medicinal products is a multifaceted task that necessitates careful organisation of interdependent processes within temperature-controlled settings, facilitating safe storage, packaging and global distribution until the patient receives the treatment.

The most significant environmental parameter having the potential to impact the quality of a pharmaceutical product is temperature.[1]

The supply chain logistics of a clinical trial risk compromising medicine integrity if temperature excursions are not handled systematically. While this may be considered a bare minimum for efficient supply chain management, recent developments in drug research underline the importance of approaching the cold chain holistically. Indeed, the frozen temperature requirements of biologics combined with the persistent need to be cost- and time-efficient are driving a new perspective in the cold chain process of clinical supply management.

Contextualising the cold chain: a growing demand

The healthcare sector is increasingly shifting its attention to harness the potential benefits of pioneering advancements in emerging medical fields such as cell and gene therapies (CGTs), particularly for patients with rare diseases. Propelled by technological breakthroughs in research methodologies, we now witness a global surge in next-generation clinical trials. Notably, there has been an industry shift from small molecules in clinical research towards biologics. According to one of GlobalData's latest reports, it is projected that the sales of biologics will surpass those of innovative small molecules within the next five years, with biologic sales expected to exceed small molecule sales by a substantial $120bn by 2027.[2]

Biologics in practice: 'ultracold' chain management enabling drug launches

Biologics, in practice, stand apart from traditional small-molecule drugs due to their unique characteristics and requirements. Biologics require specific handling as they are less stable than chemically derived drugs – the critical differentiator between biologics and traditional medicines being their need for stringent ultracold temperature conditions (most often at -60°C and below). This is crucial to ensure these materials' integrity over time, as temperature deviations can lead to product degradation, loss of potency and compromised trial results.[3]

As more and more clinical trials move toward temperature-sensitive biologics, there is a growing need for service providers to ensure that temperature thresholds remain consistent throughout their journey from manufacturing to storage, transportation and to the clinical site in an efficient but also cost-effective manner. Simply put, time is money, and that adage cannot be truer in the competitive industry that is pharmaceuticals. By putting in place a supply programme that shortens timelines and cuts costs overall, clinical supplies management providers can be pivotal in helping sponsors get to market before their competitors.

Ensuring clinical trial success

Biologics-based therapies often possess limited stability data and a short shelf-life, necessitating strict temperature control. To mitigate risk, the optimal approach is to collaborate with external clinical supply professionals with the knowledge, expertise, well-established standard operating procedures and robust systems to ensure the sensitive products are handled according to their specific requirements. In light of the intricate nature of maintaining ultra-low temperatures in the cold chain, sponsors are now actively seeking out partners who go beyond simply fulfilling storage or packaging requests. Pharmaceutical companies and biotechs are looking for an advisory approach from their clinical supplies management vendor. An ideal provider will have extensive experience managing the entire cold chain for advanced therapy drugs and will be able to proactively advise on the best option to implement for a particular challenge. If they are well versed in adapting to cold-chain requirements and their associated challenges, the provider will act as an advisor prior to trial kick-off and be able to tailor a supply programme to the needs of the project. This approach can include advising on and implementing various technologies and methodologies to optimise the supply chain, the most suitable packaging or labelling methods, as well as ideal distribution routes to guarantee product safety.

Industry best practices

As biologics and advanced therapies become more prevalent, these temperature-sensitive compounds challenge conventional logistics. Managing the cold chain introduces many risks and uncertainties, ranging from temperature fluctuations during transit to unforeseen delays in the supply chain, any of which can lead to jeopardising the integrity of these life-changing therapies. The following factors should therefore be considered when selecting a logistics partner for an advanced therapy trial.

The ability to adapt quickly

Clinical trials are characterised by their ever-fluctuating nature. Studies often witness shifting supply allocation requirements and changing study protocol. Speed and flexibility are essential for keeping the study on its intended course. While many larger organisations lack the flexibility within their teams to adapt to changing client needs or changing environmental conditions (think distribution to countries with hot climates), a client-centric clinical supplies partner armed with extensive knowledge of packaging, labelling and distribution complexities should respond promptly to requests and possess the agility required to navigate the challenge effectively. Sponsors may ask for concrete examples of such flexibility when seeking out a clinical supplies partner. In addition, certain specific clinical supply services may be suitable for trials with the need for a great deal of flexibility. For instance, selecting a logistics partner that utilises on-demand packaging may aid in shortening clinical trial timelines and reducing costs.

Global reach

Regarding low-stability drugs, sponsors should prioritise partners equipped with clinical trial facilities strategically located across critical geographic regions on every continent. This strategic geographic coverage enhances cost efficiency and streamlines supply planning while bolstering flexibility. The ever-expanding landscape of emerging markets (China, Brazil, India and South Africa) as well changes in study design due to geopolitical climates further underscore the necessity of relying on global capabilities and flexible supply routes. In 2022, the Asia Pacific region (APAC) accounted for 57% of phase 1 and 49% of phase 2 trials worldwide.[4]

Consideration of innovative solutions

A notable challenge for cold chain integrity frequently emerges when labelling at temperatures as low as -60°C is required. Providing a labelling solution that meets the technical challenges associated with its application over dry ice during packaging and labelling is complex. Most labels currently available on the market often fall short, lacking the ability to adhere effectively to vials in such extreme environments.

> *Pharmaceutical companies and biotechs are looking for an advisory approach from their clinical supplies management vendor*

Sponsors should ensure they work with a clinical supplies partner experienced in identifying and executing solutions for labelling options that comply with the rigorous logistical constraints of packaging and labelling in ultracold conditions.

Catalysing innovation through secure clinical supply chains

A dependable clinical supplies provider doesn't just fulfil a task; it assumes the role of a strategic partner and is dedicated to working with the sponsor to craft a strategy tailored precisely to the requirements of the study. This can involve introducing innovative approaches to managing the cold chain, such as artificial intelligence (AI), where relevant for the sponsor. Advanced technologies utilising AI are now being employed in most industries to improve productivity. 46% of supply chain executives anticipate AI becoming the most significant investment area within the next three years.[5] The clinical supplies space is not an exception.

Integrating AI and machine learning into cold chain supply management brings a transformative shift to the pharmaceutical industry. Thanks to powerful data-driven algorithms, generative AI technologies can help optimise supply routes, offer enhanced visibility on product temperature during transit, automate processes, shorten timelines and reduce costs. To provide a concrete example, AI can help predict an individual patient's likelihood to advance to a higher dose (and hence indicate the need for increased supply).[6] What's more, by leveraging AI capabilities, clinical trial sponsors can drastically reduce waste and minimise their carbon footprint. Advancements in AI undeniably hold the potential to enhance operational efficiencies and reduce costs associated with cold chain logistics. However, the technology doesn't provide an out-of-the-box solution to clinical supplies management. It is essential to recognise that the true power of AI emerges when it is harmoniously integrated with profound industry expertise and applied experience. This synergy will undoubtably catalyse innovation in the pharmaceutical sector.

Keeping up with advanced cold chain management technologies and techniques is an indispensable pillar to reducing risk and thus ensuring success for clinical trials involving biologics. The increasing importance of real-time temperature data management, for example, cannot be overstated, as it empowers swift decision-making to ensure clinical trial integrity. While it is impossible to eliminate the potential for risk in advanced therapy trials, the careful selection of clinical supplies management partners with cold chain management experience, industry expertise and the technologies and processes best suited for ultracold conditions can significantly minimise their impact. By enabling sponsors to adhere to their product's handling requirements, clinical supplies partners can be instrumental in facilitating access to innovative medicines for patients worldwide.

References

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Gunter Van Hoof is VP of EU Operations at **Clinigen** and oversees the clinical operations at Clinigen's German and Belgian locations. Gunter has built up over 21 years of clinical operations experience executing GCP/GMP processes with an expertise in end-to-end supply chain, clinical supplies packaging and labelling, and global distribution aspects. Gunter recently spoke at the Global Clinical Supplies Group European Knowledge Forum, where he discussed assuring product integrity throughout the cold chain.

Clinigen: true experts in clinical supplies

Clinigen combines market-leading clinical trial supplies such as packaging and labelling, global storage and distribution with, comparator sourcing as well as biological sample management services

Part of a global supply chain facility and depot network, the Clinical Supplies Management team delivers tailored solutions for clients to ensure their clinical trials are a success, regardless of project size, scope or stage. With over 25 years of experience, Clinigen acts as a pathfinder for innovative medicines – offering custom solutions designed for agility and delivering industry best cycle times.

Tailored clinical trial services

Clinigen partners with pharmaceutical companies and biotechs to install and tailor supply programmes that meet the exact needs of each clinical trial, including logistics planning, comparator sourcing, storage, inventory control, packaging and labelling and distribution. Experts in cold chain management, Clinigen is well versed in advising clients on the most optimal supply routes and advanced technologies to ensure product integrity.

Flexible packaging and labelling methodologies

On-Demand is the packaging and labelling of clinical supplies specifically for, and immediately prior to, each shipment request. With Clinigen's On-Demand method, sponsors can shorten timelines, reduce waste and increase the flexibility of their study. On average, 50% of all clinical supplies that are packaged and labelled are never used. As wastage is a major source of added costs for trial sponsors, expensive and limited supply medicines in particular can greatly benefit from the On-Demand method.

Safe and cost-efficient biological sample management

Clinigen offers biorepository services ranging from short- and long-term biological sample storage of samples collected during a clinical trial to the management of a client's entire biorepository. Biorepository services include storage infrastructure, flow management and management of sample demographic data. With owned storage facilities in the US and Europe, they cover a wide range of cold and ultracold options, with 24/7 temperature monitoring. They also provide bar-coded scanning and their unique over-tubing process.

Clinigen guarantees competitive pricing (there are no premiums for unique or small storage projects) and custom solutions for clients, regardless of the number of stored biological samples.

Market-leading comparator sourcing

As a market leader in Comparator Sourcing, Clinigen offers smart and flexible strategies to provide trial sponsors with unrivalled access to medicines and ancillaries, as well as direct access to a global network of manufacturers, audited third-party suppliers and approved distributors. Clients benefit from their exclusive and preferred-partner relationships with manufacturers and their valuable local and global knowledge across the manufacturer landscape.

IIS services

Thanks to decades of experience providing Investigator-Initiated Studies Services, Clinigen's unique perspective enables it to implement smart and flexible processes that operate as if they were outside a clinical study. When it comes to distribution, it has managed regulatory pathways required to facilitate the movement of materials in support of IIS and EAP programmes at an international level.

Whether it serves as its client's clinical supplies department or augments its in-house capabilities through its clinical services, Clinigen provides one point of contact, one solution and one contract. Rather than just processing orders, its teams' deep industry expertise enables it to deliver an advisory approach to ultimately accelerate its client's journey through clinical development, so that the product can reach more patients and touch more lives.

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