Case Study

Harnessing effective cold chain capability to absorb the impact of mid-study protocol changes

The most successful clinical trials have one thing in common: their sponsors never stop looking for ways to improve and refine processes that support the core objective of delivering safe, compliant investigational product to patients, when and where they need it.

For sponsors operating global studies involving temperature-controlled drugs, the need to embrace continuous improvement in a bid to reduce supply chain complexity is a pressing one. Opportunities to reduce the risk of temperature excursions, and the delays, negative patient impact and additional cost associated with them, are plentiful. These opportunities include fine-tuning distribution strategies to effectively balance drug conversation against cost, embracing innovative labelling practices, and using dry ice to maintain stability criteria.

Yet the drive to continuously improve can often lead to mid-study protocol amendments. When combined with the large-scale and complex nature of a global biologics study, this can have a counterproductive impact and cause untold disruption, if sponsors fail to develop an effective strategy to manage change.

One global pharmaceutical company, with a passion for innovation and dedication to addressing diverse medical needs of patients around the world, was working to refine its trial drug formula without disrupting its live global, phase II study. With over 50 sites and 200 patients, the pressure was on to react quickly and adapt temperature-controlled packaging and distribution strategies, without inconveniencing patients or falling behind key study milestones.

The Business Challenge

Mid-study protocol change risks study disruption

The sponsor's trial commenced with drug supplied in frozen liquid form, contained in vials that needed to be stored at -20°C. To make the drug easier to store and ship, the sponsor was working on changing the drug formula; removing water from the material and dry freezing, to create a lyophilized powder that could be stored at temperature ranges of -2°C to -8°C. This formulation could then be reconstituted to its original form for injection at the clinical site. The sponsor planned for all patients already enrolled in the study and receiving the drug in its original formulation to transition to the lyophilized product when it became available.

However, when the lyophilized drug was approved for use mid-study, regulatory feedback demanded that existing patients would need to continue receiving their treatment drug via its original formation. With new patients enrolling in the study, existing cold chain frameworks would need to adapt quickly to accommodate two separate supply chain approaches for the frozen and refrigerated drug supplies.

Although the two formulations were technically the same active ingredient, the two presentations would need to be treated as unique products from an operations perspective. Each would require very different packaging, labelling and shipper technology to meet the different temperature requirements from production line to patient.

The sponsor needed to develop a second kit type and packaging to accommodate the lyophilized powder. This would require the design and creation of new cartons,

inserts and labels. Making the two supplies visually different was a key consideration to ensure that the two separate kits were each stored in correct temperature ranges while at the clinical site.

Finally, when a shipment request was raised for both product forms, the sponsor would need to effectively co-ordinate packaging and distribution activity for both formulations to ensure sites received the right combination, under the right conditions, at the right time.

What started out a positive action that would improve and streamline the sponsor's trial was now running the risk of introducing even more operational complexity and disruption to patients.

The Almac Solution

Responding to change with expert cold chain capabilities

To successfully embed the dual formulation within the trial's clinical cold chain operation, the sponsor drew upon the meticulous supply chain management, project management and expert capabilities of its clinical services and technologies partner, Almac.

Working in close collaboration with the sponsor's clinical and supply chain teams, Almac experts devised methodologies to effectively manage the transition from frozen to lyophilized kits and for the distribution of both formulations. Core to this was Almac's Interactive Response Technology, IXRS®. This redesign was critical to ensuring continuous patient supply and required integrated forecasting and site inventory management data to create the optimised supply chain. Almac's expert supply chain management team also modified the IXRS to accommodate both drug forms by, for example, adjusting re-supply triggers to minimise the risk of overage.

Finally, Almac analyzed the existing distribution strategy against the new criteria of the mid-study protocol change. To successfully incorporate the new temperature ranges and demonstrate each product's integrity, Almac utilized its iTag temperature monitors. These devices enabled individual sites to download temperature reports via USB when receiving shipments. When integrated with TempEZ™, Almac's proprietary temperature management software, this provided the sponsor with a holistic view over all temperature data from product manufacture to patient administration.

To cater for the different temperature ranges required and minimise the risk of excursions occurring in transit, Almac recommended use of its Almac Pod™ temperature-controlled shipping solution. The frozen shipper was used for the original liquid formulation, while the refrigerated shipper was selected for the lyophilized powder product. Both would mitigate the risk of temperature excursions through the inclusion of phase change materials that provide 96 hours temperature protection to contents.

The results

Fast, decisive action and collaboration prevent delays and disruption

Despite introducing a duel formulation aspect mid-study, the sponsor's trial continued with no delays or interruptions and with zero negative patient impact.

Sites received shipments on time and under the correct temperature parameters, which empowered clinicians to promote positive patient experience and support enhanced retention.

Thanks to Almac's fast, decisive and collaborative approach to problem solving the issue, the trial's digital and physical supply chains were successfully adapted and unified to create a tailored, bullet-proof cold chain operation. Overage was minimised, temperature excursions were managed, patient supply was streamlined, and compliance with cGXP and GDP regulations was upheld.

Crucially, with support from its longstanding partnership with Almac and close collaboration of operational and supply chain processes, the sponsor was able to close patient recruitment ahead of schedule: supporting its mission to contribute to the enrichment of quality of life around the world, through the creation of innovative pharmaceuticals.

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