ALMAC

Partnering to Advance Human Health

Case Study

Formulating the blueprint for effective clinical labelling in ultra-low temperature conditions

The emergence of biologics has contributed towards impressive advancements in the treatment of multiple disease types; offering improved quality of life and better health outcomes to millions of patients worldwide.

Manufactured in, extracted or semi-synthesized from biological sources, biologics offer an effective therapeutic alternative to traditional pharmaceutical products. Yet, they also present several operational challenges to the clinical trial organisations developing them. Biologics are highly temperature-sensitive, with a cumulative stability budget, the absence of an effective excursion management process throughout the supply chain can create unwanted consequences for both patients and manufacturers.

Maintaining precise temperature conditions throughout a drug's cold chain lifecycle isn't an easy task. It is a task that requires expertise of the best practices and knowledge of what to do when things don't go as planned. It is important to remember that at the end of every pharmaceutical cold chain, there is a patient and it is imperative that the drug reaches them in the right condition and at the right time.

More specifically, when it comes to the clinical labelling processes of biological products, operating within ultra-low temperatures can present many barriers to success. Processes that, at face value, can seem straightforward at best and insignificant at worst, have the potential to interrupt drug supply and demand. Add to this the relative immaturity of the market, and the expensive nature of the products, developing blueprints for effective clinical labelling of biologics becomes vital. Timing is everything. Supply Chain Managers and the packaging specialists must consider all factors that could result in unexpected events that could potentially jeopardise the quality of the product and must implement strategies to proactively address them.

For one publicly-owned biotechnology company, developing biological products for the treatment of eye diseases, the need to maintain ultra-low temperature conditions was a necessity but came with many challenges.

The challenges – operating in extreme controlled storage conditions

Operating its phase II and phase Ib and 2a studies, the sponsor's drug product required extreme controlled storage conditions at -80°C. Given the potential for error, it is essential to have a concrete control system in place that can both maintain the required conditions as well as respond quickly to address any potential temperature excursions. Even though the drug had limited out of scope conditions permitted, this was only down to -60°C, which still presented two core challenges.

The first challenge related to labelling the sensitive materials. Labelling traditional drug products in ambient temperature environments can be very straightforward. However, if drugs need to have labels applied at temperatures lower than -20°C, there are limited adhesives available that are capable of effectively bonding labels to the packaging. Standard adhesives freeze solid before a bond can be made with the surface of the packaging rendering them useless. They must be capable of withstanding these extreme low temperatures while retaining full adhesion once the trial products are ready to be used.

If the label is applied in an ambient environment and then placed into a freezer, the bond will have already formed, making standard adhesives an appropriate solution in this scenario. This unfortunately wasn't an option for this particular sponsor, due to the extreme temperature conditions that needed to be maintained to safeguard drug efficacy and compliance.

The second challenge related to the labelling processes. With the rise and diversification of biologics in recent years in an emerging market, there was no tried and tested blueprint available for the sponsor to develop an effective labelling strategy, establish health and safety protocols, manage risk or formalise SOPs for operatives.

Working with incredibly expensive drug products, mistakes would be costly and not only risk negative patient impact but, for a listed company, potentially damage investor relations too.

The Almac solution – sourcing appropriate materials, building an effective strategy

To ensure the success of this vital study, the company turned to Almac to solve the problems standing in the way of effective and compliant clinical labelling processes.

Almac's Clinical Services division quickly began investigating multiple markets and suppliers in a bid to source an appropriate adhesive. The research established that a suitable adhesive, capable of forming a bond at the extreme temperature conditions required, was not available anywhere in Europe. Extending its search, and utilising its global reach and local expertise, Almac identified a suitable product and supplier in the United States.

Procurement of the right materials was the first part of the battle. The next step was to develop a strategy for the unknown; to establish a method of safely and effectively applying labels to hundreds of glass vials, between -60°C and -80°C.

Limiting the time the drug spent outside of its optimum temperature of -80°C was top priority. Dry ice was the chosen solution and is the most commonly used and reliable refrigerant to keep products in their frozen state. The Almac team then established a mechanism using dry ice to transport the drug from the ultra-low storage freezers to the production line without risking temperature excursions above the absolute limit of -60°C.

Allocating only one minute for each label to be applied to a vial before being placed back in the dry ice, it was essential that the label design was both fit-for-purpose and quick and simple for operatives to affix to the primary packaging. Single tab labels and booklet labels were used to aid quick and simple application.

However, if air pockets were present between the label and the vial, the label could easily detach and fail quality inspection, resulting in heightened risk of temperature excursions and added costs of relabelling. Getting it right first time was paramount.

A full risk assessment was conducted before a safe, consistent and repeatable SOP for operatives was recommended to the sponsor. This included the use and procurement of specialist gloves that would protect operatives' hands from the extreme temperatures, prevent body heat transmitting to the vials, whilst facilitating the dexterity required to quickly and precisely apply labels. Cartons were also pre-conditioned in a freezer 24 hours prior to the labelling operations. Testing the approach with dummy product also formed part of the due diligence activity, while secondary packaging cartons were labelled as standard within ambient environments.

The results – 100% compliance with extreme temperature conditions, zero quality issues

Rising to the challenges posed by the extreme temperature conditions meant bringing together the experience, knowledge and strong supplier relationships of Almac's global clinical labelling experts.

By always keeping the patient in mind and by adopting a solutions-focused mentality to respond to a unique set of requirements, Almac was able to source a rare adhesive and deliver a safe, effective and compliant labelling strategy for the sponsor. In doing so, a proven blueprint for clinical labelling of drug products with extreme temperature conditions has been established, which will offer enhanced speed and agility for the sponsor's subsequent activity.

All kits were successfully labelled, with no temperature excursions. As a result, the best practice approach to clinical labelling activity proved a crucial component in helping the sponsor meet its study's key milestones, maintain investor relations and, most importantly, continue developing revolutionary therapies for the treatment of eye diseases.

By empowering decision making and providing continuous process improvements to sponsors and sites, this best practice approach will ultimately provide sponsors with complete confidence that their drug is safe for the patient.

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