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CASE STUDY

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The critical importance of comparator temperature excursion management

A robust quality assurance process

Comparator procurement is one of the most expensive components of clinical trials. This cost takes on further meaning as the risk of a temperature excursion or a loss of drug due to time out of environment can result in additional charges and potential delays in the trial.

The impact of inconsistent site equipment

A leading biosimilar company was running a phase II trial with a large molecule drug for the treatment of rheumatoid arthritis. Thermo Fisher Scientific was in charge of the comparator sourcing, packaging, labeling and distribution for the trial.

The packaging and labeling of the Investigational Medicinal Product (IMP) and the reference medicinal product was performed in a walk-in refrigerator so that the drugs remain at a consistent temperature.

The challenge

Storing and transportation to the individual clinical sites was performed as scheduled within the required temperature range. Unfortunately one clinical site had a defective refrigerator for where, for 34 minutes, the drugs were stored between 8°C and 12°C. If these medicinal products are exposed to temperature outside their approved range of 2°C to 8°C (up or down), they can, at best, lose their effectiveness and, at worst, aggregate into particles that can cause serious reactions in patients.

Thermo Fisher Scientific's Quality Assurance (QA) Team investigated immediately to find out if the reference product could still be used even though it had been stored outside the required 2°C to 8°C range. Unfortunately this product had no published stability data, neither in the electronic Medicines Compendium nor in the FDA database.

The solution

In order to get clarification, our QA Team contacted the manufacturer. Thanks to the excellent relationship with the manufacturer and the fact that the product was sourced directly from one of its warehouses (with no intermediary), we received the response to our request and the assessment of the excursion in a very short time. Consequently our QA team was able to issue a “Fit for Use” document on the same day.

In parallel, the biosimilar sponsor informed the clinical site that, according to its stability profile, the IMP could still be used. After receiving this confirmation, the clinical site was able to continue with the trial and avoided the time intensive and expensive resupply scenario.

Cooling the self-cooling delivery

The Thermo Fisher Scientific Comparator team supplied a global U.S.-based pharmaceutical company with an oncology drug sourced in Europe that was to be imported to the U.S. for further processing.

According to our standard processes, we prepared and supplied all necessary documents in advance to U.S. Customs in order to guarantee a smooth border crossing. After receiving the confirmation by U.S. Customs that the document satisfied their requirements, the shipment process was initiated. The products were packed into qualified shipper boxes configured for 2°C to 8°C products in order to guarantee a cold chain throughout the journey. The shipment was packed with chilled packs at +5°C and as well with frozen packs at -20°C in order to remain within range for 72 hours when stored at an ambient temperature. According to GDP, the products were tracked by multiple data loggers during the shipment and the temperature was recorded as within specifications.

The customs clearance process can be fairly unpredictable across the globe. In this case, the Customs team had a question for the sponsor that introduced a delay.

Temperature decreased to 0°C when stored at 5°C

A customs officer noticed that the shipment required temperature management at 2°C to 8°C and, as a result, placed the packages into a properly working refrigerator at 5°C. As the packages were configured for an ambient temperature and their contents were cooled with frozen packs (at -20°C), the temperature of the drugs began to decrease in the refrigerator. Once the shipments cleared and were delivered to the site, the data logger revealed that the products were stored at almost at 0°C for 10 hours.

The solution

Thermo Fisher’s Quality Assurance team contacted the manufacturer for clarification and received a same-day response. We were approved to issue a “Fit for Use” document and the comparator drug was ready to use. As patients were already waiting at the clinical site for their treatment, the fast clarification allowed us to keep the clinical trial on track.

To ensure proper handling at the investigator site, the Thermo Fisher Scientific team always applies additional labels with storage instructions that clearly identify temperature requirements.

Conclusion

When working with Comparators, the required support extends well beyond sourcing. The product is often most at risk during the delivery to or from the packager or from the innovator. To maintain the highest possible quality throughout the supply chain, leveraging expertise beyond comparator, like packaging, shipment or Quality Assurance support is crucial.

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