

Technology Solutions for Challenges in Cold Chain Supply Management

by Timothy S. Brewer

Introduction

Clinical trials of large molecules are increasing by double digits and make up nearly 30% of the current drug development pipeline. The sensitive nature of biologics, typically stored in glass vials in cold storage, renders any product useless only minutes “out of the environment.”

Increasingly, clinical trials are conducted outside of traditional markets, further driving complexity in the packaging, storing, and transporting cold chain and other temperature controlled products.

The purpose of this *Knowledge Brief* is to give an overview of the newest technologies that offer solutions for the growing challenges in cold chain supply management. Specifically, this *Knowledge Brief* will discuss four new technologies – phase change materials, global positioning systems, RFID, and USB drives – and evaluate their potential for success.

The Challenges

Companies investing millions in the development of costly biologics cannot

afford a single vial to go to waste nor miss a treatment window with a study participant due to shipping delays or potency-destroying temperature fluctuations during transit. The molecules used are very sensitive to temperature fluctuations and must be maintained with a specific temperature range of +/- 2°C.

More and more clinical trials are being conducted outside of traditional Western markets – both to reach larger naïve patient populations and to cut costs out of the development process. Ensuring that therapeutic products make it to investigator sites within established stability limits requires a proactive planning approach and innovative use of technology to protect a pharmaceutical or biotech company’s investment in their product.

Additional shipping time to reach new geographic areas and the need for specific local regulatory expertise and understanding of the proper import licensing and other entry requirements of non-Western countries adds more layers of complexity to the global logistics and transportation process. Addressing these

challenges as the industry moves to new regions is driving most pharmaceutical and biotech companies to identify the best solutions for effective management of temperature-sensitive products.

Historically, active cooling shipping containers (essentially refrigeration units on wheels) have been the only solution for maintaining stability for sensitive products during transit. Expensive, large, energy-consuming, and inflexible, active coolers cannot be scaled to meet the variable product quantity needs of every investigator site. Additionally, active cooling solutions do not address the challenges presented by remotely located, often less developed investigator sites, nor ensure real-time, all-the-time protection and monitoring of sensitive biologics in a way that allows temperature remediation before a product is accidentally destroyed by temperature fluctuations.

Technology Solutions

The latest scientific advancements in temperature-controlled shipping use passive cooling shipping containers. Cost-effective and flexible enough to accommodate any size shipment, passive coolers keep temperature-sensitive shipments within required temperature ranges in either hot or cold ambient conditions.

Phase Change Materials

Passive coolers feature an innovative approach to controlling temperature using scientific advancements in Phase Change Materials (PCMs). The temperature ranges required by a biologic determine the selection of which PCM formulation to use. PCMs can consist of any combination of patented materials.

Unlike conventional shipping materials, when PCMs reach the temperature at which they change phase (either melting or solidifying temperature), they absorb or release amounts of energy (hot or cold), at an almost constant temperature. When the ambient temperature around a liquid material falls, the PCMs solidify, releasing their stored latent heat. If

the temperature rises, they liquefy and release cold. The PCMs will continue to absorb energy without a significant rise in temperature until all of the material is transformed to the liquid or solid phase, depending on whether the PCM is protecting a product from heat or cold.

PCMs also permit light-weight packaging with the maintenance of temperatures in narrow, preselected ranges. They can extend the length of time a product can be in transit and increase the ability to ship product to farther distances, while ensuring the product arrives at an investigator site in perfect thermal condition and within its required temperature stability range. No longer are sponsors limited to shorter shipping distances. PCMs increase the storage and shipping time of a product from 48 to 96 to more than 120 hours, allowing treatment of patients who would have otherwise never have access to these products.

Additionally, for companies who have made a commitment to decreasing their carbon footprint, passive shippers offer a safe, reusable, and non-toxic solution that reduces waste and energy consumption with every shipment.

Global Positioning Systems

Monitoring is critical for ensuring that a product maintains the right temperature throughout its life in storage or during the shipping journey. Advances in packaging design now include Global Position Systems (GPS) shipped inside passive coolers alongside the product that are programmed to send clinical trial project managers real-time, all-the-time temperature monitoring of a product, as well as offer precise shipment tracking. This allows temperature adjustments to be made during shipment when temperatures start to track out of specification. Repackaging or reshipment ensures that sites receive acceptable drug in time for patent administration.

Universal Serial Bus

Tracking temperature changes throughout a product's lifecycle has

been made faster and easier using Universal Serial Bus (USB) to download temperature monitoring data. Tracking devices allow the user to plug into any USB hub, from a desktop to a laptop, and download a complete temperature profile from time of origin through delivery confirmation.

Radio-Frequency Identification

Radio-Frequency Identification (RFID) chips further expand monitoring capabilities by allowing a delivery agent to scan a shipping container and send temperature monitoring information immediately to the clinical trial project manager confirming successful temperature-controlled shipping without even opening the shipping container.

Conclusion

When it comes to managing the supply chain of temperature-controlled products throughout packaging, storage, and transportation to investigator sites, protecting these sensitive biologics requires innovation and all-time-time attention to real-time information. Any breakdown in cold-chain protection or miscommunication of vital temperature information can destroy a product or invalidate a patient from the study population. In this economy, no degree of error is acceptable – or safe.

For Further Information

For more detailed and related information, the following ISPE resources are available:

Technical Document:

- ISPE Good Practice Guide: Development of Investigational Therapeutic Biological Products <http://www.ispe.org/goodpracticeguides>

Recorded Webinar:

- Overcoming Regulatory and Logistical Hurdles When Conducting Clinical Trials in India <http://www.ispe.org/onlinelearning>

Investigational Products (IP)**Community of Practice (COP):**

- Visit our IP COP on the ISPE Web site for the most current and up-to-the-minute discussions on the topic discussed in this *Knowledge Brief* and other related topics.
<http://www.ispe.org/communitiesofpractice>

About the Author

Timothy S. Brewer is Global Vice President, Logistics at Fisher Clinical Services. Formerly Chief Executive Director of Clinical Trial Services (CTS), Brewer has more than 15 years of experience in the pharmaceutical industry. He established CTS, a pharmaceutical packaging firm, in December 1996 where he was responsible for providing executive leadership, managerial direction, and client development. Brewer attended the United States Military Academy at West Point where he majored in chemical engineering, and Alvernia College where he received a BS in business administration and management. He is a member of various professional organizations, including the Drug Information Association (DIA), Association of Clinical Research Professionals (ACRP), ISPE, AAPS, and others. ●