From Risk to **Regulatory Approval**

How Cryoport Systems Validated a Shipping Solution, Enabling CGT Commerial Launch

Case Study

Cryoport Systems

Americas • EMEA • APAC
info@cryoport.com | +1 949.232.1900
cryoport.com

When a client came forward with a third-party shipper line that didn't meet compliance standards, Cryoport Systems' Consulting Services proposed enhanced shipper designs that would allow the shipper to perform according to the required thermal, shipment, and safety standards to support the commercial launch of a leading biopharmaceutical company's lifesaving product.

Background:

A leading biopharmaceutical company was preparing for the commercial launch of their cell therapy and required timely and thorough qualification of their third-party self-cooling shipper* to ensure the safe transport of their vital therapy. To transport their product compliantly at the necessary temperature range and meet established standards, they elected to partner with Cryoport Systems' Consulting Services team to qualify the client-selected self-cooling shipping system and meet the critical commercial launch timeline.

Cryoport Systems' Consulting Services team is comprised of Validation Engineers, Packaging Engineers, Data Service Engineers, and Program Managers. The Consulting Services team specializes in identifying risks throughout the global life sciences temperature-controlled supply chain by qualifying and proposing solutions that protect and streamline a client's temperature-sensitive supply chain. Consulting Services' offerings include thermal and physical shipper qualifications, shipping risk assessments, shipping lane validation, packaging validation, packaging/accessory design and implementation, data services, trade services, and other customized development and qualification projects (e.g. custom shipper development, custom qualification projects, etc.). With the help of Consulting Services' expert team supported by Cryoport Systems' platform of compliant, customizable, and comprehensive solutions, organizations can make the best risk-weighted decisions for their vital, life-saving therapeutics throughout all areas of their temperature-controlled supply chain.

Problem:

In anticipation of commercialization, a prominent biopharmaceutical company aimed to offer hope to patients globally with their lead cancer therapy. However, it could only do so if the product arrived at their manufacturing facilities in perfect condition within a specified and qualified temperature range. The success of their product and its impact on patient lives relied heavily on the consistent performance of the company's selected self-cooling shippers that were contracted through a third party and an associated passive condition monitoring solution. The self-cooling shippers needed to maintain internal temperatures to keep the biologic materials within a very specific temperature range and withstand potential external harm during transport. With less than a month before submission, there was an extreme urgency to determine how to successfully validate the shipping system to support the biopharmaceutical company's Biologics License Application (BLA) submission, enabling them to ship their product commercially.

Solution:

To determine the third-party shipper's viability, the company chose Cryoport Systems' Consulting Services team to perform complete Operational Qualification testing of both thermal and physical qualifications that complied with International Safe Transit Association (ISTA) standards and American Society for Testing and Materials (ASTM) standards. Following Cryoport Systems' Consulting process methodology, customized protocols for comprehensive shipper qualification tests were created based on the client's acceptance criteria.

The scope of the first Thermal Qualification protocol was to determine if the shipper could maintain its marketed temperature range. The type of self-cooling shipper the biopharmaceutical company selected had been "qualified" by the manufacturer to maintain a temperature of 2-8°C for at least 96 hours from the time of activation. Six (6) shippers were tested at both standard ISTA 7E summer and winter temperature profiles. The results indicated that the selected shipper was not able to maintain the stated internal temperature range for either profile.

The second Physical Qualification protocol garnered similar results. In accordance with ASTM D4169-16 Distribution Cycle (DC) 13, the scope of the second protocol was to determine if the shipper could withstand impacts as received by packages during sorting operations and while in transit. Six shippers underwent manual handling including dropping, stacking, loose load vibration, low pressure, high altitude, random vibration, concentrated impact, and other stressors. This standardized physical testing determined that the shipper packaging was not robust enough to mitigate potential risk to the product stored inside and contributed to its inability to maintain proper temperatures.

While the results of each test had been conclusive, the outcomes were unfavorable for the biopharmaceutical company. Cryoport Systems' Consulting Services team not only understood that the findings had a substantial impact on the biopharmaceutical company but also recognized the future impact on patient lives that transporting sensitive therapeutics in a non-complaint shipper could have. To mitigate that risk, the Consulting Services team took their assistance a step further. After documenting all findings in a final report for the client, they also identified how the third-party manufacturer could enhance their shipper design to achieve a more durable and reliable shipper to meet performance requirements for the biopharmaceutical industry.

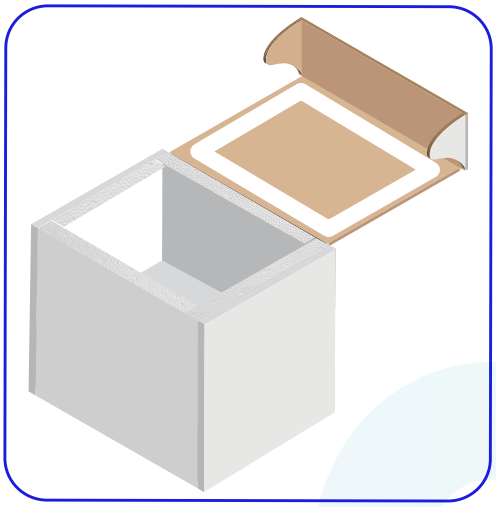

Figure 1: Illustration depicting the biopharmaceutical company's selected self-cooling shipper (exterior)

Figure 2: Illustration depicting the biopharmaceutical company's selected self-cooling shipper (interior) with packout

Outcome:

Cryoport Systems' experts used data gathered from the two tests to create designs that would improve both the shipper's thermal capacity and physical sustainability for the biopharmaceutical company and for the manufacturer. The third-party manufacturer's shipper used a self-cooling mechanism that also served as the top for the shipper payload area so the shipper would achieve the desired internal temperature over time. During testing, internal temperature ranges of the product were not consistently maintained in the client-specified acceptable temperature ranges, which would have damaged the product during actual shipment and rendered the source material not usable. The self-cooling pack unseated and released all built-up heat (cool) when undergoing physical stressors. As a result, the test materials would have been damaged during real-world shipping based on these test results.

To strengthen the third-party's shipper, the Consulting Services team designed an alternative mechanism to support the self-cooling lid, ensuring that it would remain in place even during real-world shock, vibration, and manual handling to protect the precious, irreplaceable source biologic materials upon which the therapy was derived. Additionally, it was determined that the structure's insulation allowed for heat loss. A recommendation for structural strengthening was provided to the shipper manufacturer to ensure thermal insulative integrity of the shipping system. These recommendations were presented to the biopharmaceutical company and the shipper manufacturer so that enhancements could be made to the shipping system to help the shipper maintain consistent temperatures and protect the payload. The recommended shipper enhancements were incorporated into a revised shipper design. Cryoport Systems' Consulting Services was then engaged again to qualify the suggested enhanced shipper design. Cryoport Systems' recommend enhancements to the shipper was qualified a second time following the same ISTA 7E and ASTM D4169 test standards and were proven to achieve the desired performance and maintain the temperature of the biologic product to ensure a viable sample was delivered to manufacturing. Following Cryoport Systems' recommendations, the company was then able to submit their BLA and ultimately achieve a successful commercial launch.

Conclusion:

When it came to supporting the commercial launch of a leading biopharmaceutical company's product, our Consulting Services team was able to meet the urgent needs of the client, establish a qualification baseline, identify issues with the third-party's shipper, and propose new solutions to enhance the shipper and meet the client-required thermal and physical compliance standards. Through our Consulting Services experts' advice, the third-party manufacturer enhanced their self-cooling shipper design. The biopharmaceutical company launched their product with a shipper that maintained thermal integrity, enabling the safe delivery of the therapeutic product to patients.

For reliable assistance identifying problems and their solutions within your supply chain, shipping systems, packaging, and for custom qualifications, Cryoport Systems' Consulting Services can help promote certainty throughout your processes by mitigating risk with industry-leading expertise plus decades of experience working with clients at all stage of clinical and commercial development. For more information on our custom consulting support services capabilities, please visit **cryoport.com/solutions/consulting-services.**

*The biopharmaceutical company's chosen shipper was developed and supported by a third-party company not affiliated with or a part of a product line developed by Cryoport, Inc.

About Us

Cryoport Systems is a comprehensive supply chain partner for the life sciences industry focused on meeting the challenges of the global cell and gene therapy market. We excel in the specialized management of the biopharma supply chain through our comprehensive offerings in logistics, BioServices, cryopreservation, and consulting. With our expansive platform and decades of temperature-controlled supply chain expertise, Cryoport Systems helps Enable the Outcome™ for advanced therapies programs, safely and securely guiding critical therapies to patients in need.

Cryoport Systems

Americas • EMEA • APAC
info@cryoport.com | +1 949.232.1900
cryoport.com