Biostorage:

Advanced Strategies for Ensuring Integrity in Regenerative Medicine Logistics & Storage

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Challenges Encountered When Storing and Shipping Biopharmaceutical Materials

The transportation and storage of clinical trial therapeutics and biospecimens in the biopharmaceutical industry can be complex operations that leave little or no margin for error. The integrity of these materials hinges on stringent temperature control, as temperature excursions and mishandling can compromise product efficacy[1]. These challenges persist even for the most experienced clinical trial networks and supply chain managers, where maintaining appropriate logistics and storage conditions is critical to the success of biopharmaceutical development and patient outcomes.

One of the most challenging aspects of storing and shipping biopharmaceutical materials — including bioanalytical samples, clinical trial samples, vaccines, stem cells, biomarkers, viral vectors, immunotherapies, and regenerative medicines — is maintenance of the chain of condition and chain of custody. As a logistical consideration, complete information on the chain of condition (encompassing metrics such as internal/external temperature, handling, and shock/tilt of shippers) and the chain of custody (e.g., geographical location, lane mapping, carrier performance) is critical to ensure the integrity of products during transport and storage. Any deviation from prescribed conditions can compromise the quality of the material, leading to unstable analytes or drug products, and ultimately affecting bioanalytical assay outcomes, clinical data integrity, and drug efficacy.[2]

Undocumented freeze-thaw cycles, thermal cycling, and pH changes due to improper storage/shipping conditions can result in catastrophic financial losses that put millions of dollars in biopharmaceutical products, clinical samples, and even patients at risk. The instability of analytes not only compromises bioanalytical assays but also undermines the reliability of clinical data, necessitating extensive troubleshooting and potentially years of re-manufacturing. Such setbacks can greatly delay development timelines, incurring additional costs and potentially delaying life-saving treatments from reaching patients.

Alarmingly, it is still common practice to place biological materials in a Styrofoam box with an unmeasured amount of dry ice and to hope for the best. Fortunately, advanced data monitoring and logistics systems are available to facilitate chain-of-condition and chain-of-custody maintenance. These newer systems allow biopharmaceutical companies to make data-driven logistical decisions much as they do for drug development and commercialization.

> Within the biopharmaceutical industry, the importance of a sound storage/shipping logistics strategy — and the economic ramifications of not having such a strategy — are vastly underappreciated.

Examples of Shipping Data to Track to Ensure Chain of Condition

Temperature	Tilt	Humidity	Battery Level	Pressure
-196.2°C	5°	50%	30%	14.61 psi

What to Look for in a Biostorage Partner

Selecting the right biostorage partner is crucial for ensuring the integrity and success of biopharmaceutical operations. When selecting a provider, the following elements can indicate the breadth of a provider's services as well as how those services and solutions will serve operations in the long run.

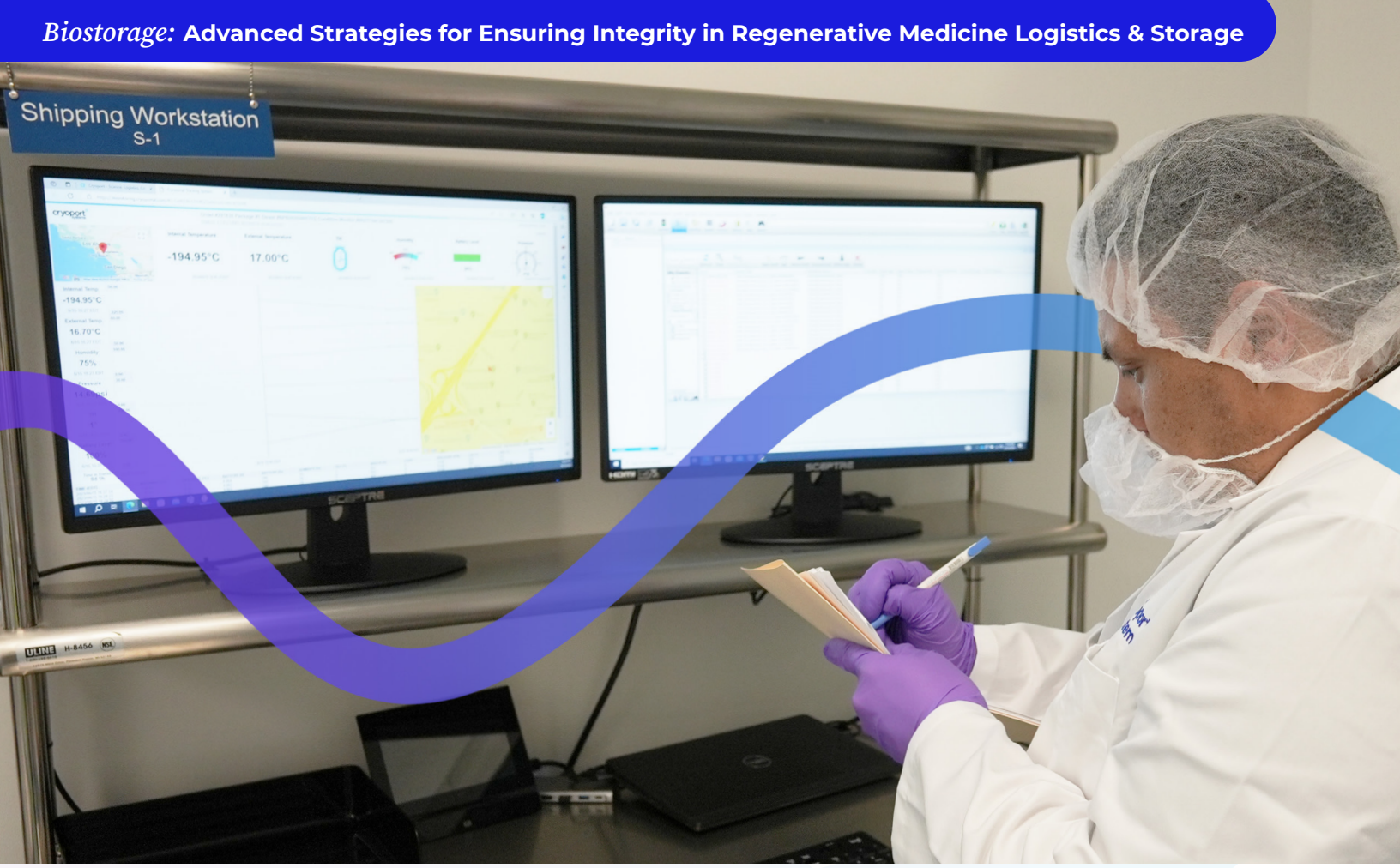
1. Adherence to Industry Compliance Standards

Compliance with current Good Laboratory Practice (GLP), Good Manufacturing Practice (GMP), Good Distribution Practice (GDP), and International Society for Biological & Environmental Repositories (ISBER) best practice are chief aspects of a robust provider. GLP/GMP/GDP/ISBER compliance means having validated cold storage equipment and freezers that are temperature-mapped and connected to backup generators as well as temperature monitoring and alarms.

2. Breadth of Temperature Bands

A second consideration is capacity and, more importantly, capacity within the required temperature bands. For example, large projects for -20°C storage may require a cold room, whereas cell lines or infectious material may require segregated cryogenic storage. A provider's temperature capabilities are equally important for storage solutions and shipping systems and include how a provider transports one to another. These elements can be condensed to a provider's sample recovery capabilities and fulfillment management. When materials are removed from storage for analysis, the conditions in which those materials are extracted and transported are of utmost importance. Storage providers must therefore access and transport materials using "cold-carts" to limit thermal cycling and analyte degradation.

> Beyond meeting immediate needs, organizations must consider the scalability of their provider as well as their personal diversification of need to accommodate projected future growth.



3. Preparation for Extreme Conditions

Other considerations come into play when biopharmaceuticals must be routed under extreme conditions such as in cold weather or tropical climates. Key factors include packaging design and performance (particularly in terms of whether performance has been validated at extreme temperatures), refrigerant volume and rate of evaporation/sublimation at given temperatures, time exposed to extreme temperatures, and a logistics and interdiction strategy to move the shipper to a less hostile environment and/or to secure the biomaterial in the event of a shipper failure. In this case, one may choose to expedite delivery, replenish the refrigerant, or move the material to a newly conditioned shipper.

4. Cloud-based Logistical Systems

In recent years, the biopharmaceutical storage and shipping field has benefited from technological advances that have greatly improved the performance and efficiency of freezers and the IT systems that support them.

To a great extent, sample accessioning and inventory management have been automated and directly integrated into a broader IT-based logistics solution, allowing for comprehensive fulfillment, shipment tracking, and data monitoring/management from a single location.

Basing logistical systems on the cloud enables transparency throughout an entire supply chain while eliminating much of the "busy work."

Such advances are facilitating the design of systems that can develop data chains to track entire histories of specific lots of drug products – while linking those histories to that of a specific patient sample – thereby enhancing data integrity and the targeting of drugs to patients who are most likely to benefit from them.

Adherence to Best Practices

Strict adherence to standards set by authoritative organizations, including the World Health Organization (WHO), the U.S. Food and Drug Administration (FDA), the International Organization for Standardization (ISO), and the International Society for Biological and Environmental Repositories (ISBER), is crucial in maintaining a secure, temperature-sensitive supply chain. Non-compliance can lead to significant risks, including compromised material integrity and regulatory penalties.

When selecting a storage and fulfillment service provider, biopharmaceutical companies should ensure their partner rigorously adheres to industry standards. The following checklist details five pillars of best practices with pertinent subtopics that can be used to assess a prospective provider.

Business Continuity and Security:

- Appropriate environmental controls (24/7), including monitoring and records
- Proactive calibration and preventive maintenance
- Redundant freezers and/or backup power plus uninterruptible power supply and backup generators
- Access policy
- Security systems
- Fire prevention/detection plans
- Emergency Response Planning
- 21 CFR, Part 11-compliant monitoring

Quality Systems:

- Documentation of current Good Practices
- Audits: records of temp, access, and inventory control
- Adequate safety measures for the type of materials stored: biological, chemical electrical fire, physical, liquid nitrogen
- Training program and documentation
  - Training records documenting frequency of training
  - Cross-training to adequately train employees on security, continuity, inventory policies, and procedures

Record Retention:

- Availability for audits and inspection

Inventory Systems:

- Current GMP-compliant storage
- Location system
- Lot control
- Audit trail/tracking
- Labeling
- Barcoding
- Temperature/humidity tracking and records

Shipping Conditions:

- Comprehensive data monitoring
- Availability of data records to validate temperature controls

End-to-end Storage & Fulfillment with Cryoport Systems

Cryoport Systems offers an integrative platform of supply chain solutions to support our life sciences clients through every stage of research, development, and manufacturing. By combining our multifaceted expertise in BioServices and biostorage, advanced shipping systems, cryopreservation services, and consulting services, we provide reliable, end-to-end storage, fulfillment, and logistics services worldwide. This comprehensive approach allows our clients to concentrate on innovation while we ensure the secure, compliant, and efficient management of their biopharmaceutical materials.

When it comes to the secure management of biopharmaceutical materials, our BioServices capabilities fulfill the life sciences industry's temperature-sensitive biostorage requirements and provide complete deliverables for clients. Housed in our specialty centers around the world, Cryoport Systems' BioServices solutions include GMP-compliant biostorage for pre-clinical, clinical, and commercial materials at all temperatures in fully validated, temperature-mapped units. These solutions possess complete traceability with end-to-end chain of identity, chain of custody, and chain of condition through our Chain of Compliance® to meet the most rigorous quality standards supporting the biopharmaceutical industry. This extends to the management of raw materials, APIs, excipients, and drug product storage in validated environments with continuous monitoring for deviations in temperature. In addition to temperature monitoring, our biostorage facilities are outfitted with automated alerts, redundant storage space, and backup generators for peace of mind and risk-mitigation of unforeseen events to protect critical materials.

Our integrated support represents a new approach to biopharmaceutical material management. These centers not only house our biostorage and BioServices solutions, but also our logistics capabilities and expanding IntegriCell™ cryopreservation facilities all at a single location to enable the support of our clients' supply chain operations. Cryoport Systems is situated as the single vendor to support centralized storage, fulfillment, and logistics processes for the life sciences within a single location. This in turn enables clients to focus more of their time and capital on their work while avoiding the substantial investment of establishing and managing their own facilities while still accessing top-tier infrastructure and resources.

References

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2. Sawicki, M. (2018, June 12). The Chain of Compliance: Why the chain of compliance is critical to winning in the RMAT market. Contract Pharma. https://www.contractpharma.com/issues/2018-06-01/view_features/the-chain-of-compliance/

The journey towards successful patient outcomes starts with complete confidence in your chosen supply chain provider. *Cryoport Systems is the trusted partner* **of temperature-controlled biostorage and supply chain solutions for biopharmaceutical materials that cannot be replaced.**

About Us

Cryoport Systems is a comprehensive supply chain partner for the life sciences industry focused on meeting the challenges of the global life sciences market. We excel in the specialized management of the biopharmaceutical 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 therapy programs, safely and securely guiding critical therapies to patients in need.

Learn more about BioServices

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