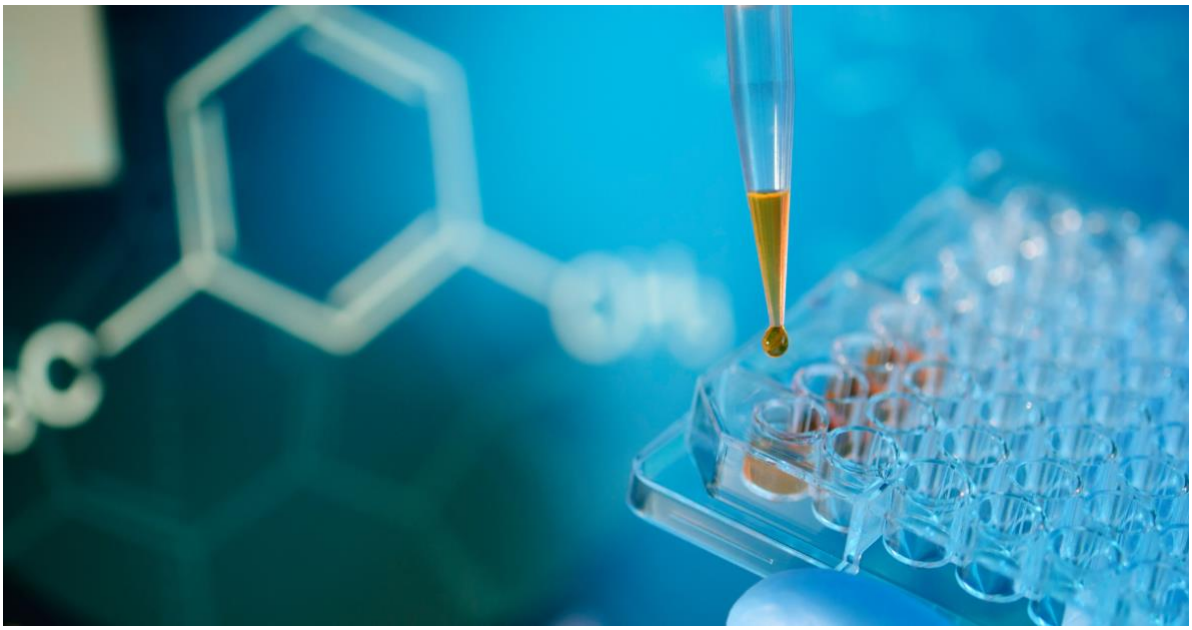
3 Fundamental Services for Superior Master Cell Bank Management



The consistency of controlled conditions is vital throughout every step in producing advanced therapies, and the process usually begins with the secure handling and storage of the cells used for manufacturing. Production of master cell banks (MCBs), safe handling, and storage can be condensed to six critical components: "specialized expertise, optimal equipment and environment, appropriate quality controls, constant monitoring, close communication, and continual troubleshooting."[1]

For those searching for a supply chain provider with the capacity to manage master cell banks (MCBs), selecting an organization that can uphold these elements is crucial since the integrity of the finished drug product relies on the quality of the starting material. Cryoport Systems' meticulous management services for MCBs set us apart from competitors and align to uphold the necessary qualities of a safe and sustained cell bank through primary and secondary risk mitigation storage activities.

1. **Storage Facilities Built for Longevity**

Master cell banks are established for the longevity of a product, and ensuring that longevity is achieved hinges on superior storage facilities. With this in mind, the FDA outlined an industry guidance report for the characterization and qualification of cells and other biological material used in the production of advanced therapies. In it, they emphasize the importance of a proper storage environment for MCBs, stating that cell banks should only be stored under conditions that are validated for long-term stability.[2] This environment consists of facilities with state-of-the-art storage systems and unfailing back-up power systems in place. Without a setup built for risk-mitigation, a provider is leaving the viability of a client's cells up to chance and risking an

unforeseen accident or external challenge such as a natural disaster that may damage an entire collection.

Robust risk-mitigation tactics are the foundation of a prepared facility. Cryoport Systems' integrated global supply chain centers (GSCC) are a first-of-its-kind facility system that contains connected services for the life sciences supply chain. Specifically designed in response to industry manufacturing needs, this type of facility encompasses our temperature-controlled logistics services with specialized storage and distribution solutions to support developers' rapidly growing service requirements. Currently located in Houston, Texas and Morris Plains, New Jersey within the United States, Clermont-Ferrand, France and Pont du Chateau, France, these centers house tanks designed by our sister company under the Cryoport, Inc. banner, MVE Biological Solutions. They are a leader in cryogenic storage solutions specifically for long-term biological material storage like master cell banks. The breadth of MVE's systems offers clients a multitude of options to choose the storage best fit for the needs of their master cell bank and overall operation.

- **The MVE High-Efficiency Series** – offers ultra-cold vapor storage of -190°C and is equipped with the TEC3000 controller, which allows for the programming of unique settings like liquid level detection and password access so that clients can be assured that only they have access to their cells.
- **The MVE HEco™ Series** – offers vapor storage at -190 °C with streamlined LN2 plumbing and vacuum-jacketed transfer hose, giving clients maximum storage density while still being one of the most eco-friendly vapor freezers available to help reduce carbon footprints.
- **The MVE Fusion®** – offers storage at -190 °C and is equipped with our innovative Qdrive cryo-cooler technology to keep samples at-temperature without needing an ongoing liquid nitrogen supply or a connection to an external source to create self-sustaining, consistent dry storage even in a power outage.

Our GSCCs continuously monitor each storage tank with a cloud-based monitoring system utilizing NIST traceable calibrated PT100 sensors. Plus, these facilities are equipped with redundant, back-up storage units with emergency generators to prevent loss of material due to unforeseen power outages. Our emphasis on reinforced safety measures means that our clients can trust the power of our GSCCs to protect their cells even in the event of circumstances that risk material viability.

2. Teams Prepped for Quick Response Time

While a superior storage facility is essential in managing master cell banks, the power of a top-notch storage facility is only as strong as its trained personnel. Proper employee training and processes is an imperative responsibility for the establishment of good manufacturing practices (GMP) in the handling of sensitive materials and advanced therapies.[3] This extends to the personnel's confidence in their ability to handle the complexities of servicing the manufacture of advanced products. Standard Operating Procedures (SOPs) should be in place to cover all possible scenarios from routine to last-minute requests so that employees can navigate fulfilling the requests properly and in a timely manner and without the risk of contaminating the material.

Cryoport Systems' teams are trained to handle all equipment and procedures according to GMP regulations. Our SOPs and procedures are uniform across all Cryoport Systems' locations, meaning that a client's sensitive materials will be handled according to the industry's highest standards (ISO 21973, ISO 9001, etc.) no matter the location. Additionally, the strategic location of our GSCCs provides a unique advantage for our clients storing their cell banks with us. Our Houston and Morris Plains facilities are co-located with our global logistics centers so that our team can flawlessly transition stored material to a shipping system prepped for transport in a matter of hours. This means that our team members can physically walk a temperature-controlled transport tank from the storage building to the logistics center without risking temperature stability. Our streamlined process removes the overall number of legs from facility to transport, making quick turnaround times possible without cutting corners.

3. Meticulous Record-keeping Technology

Furthermore, the risk of contamination due to fluctuating temperatures is of major concern for developers and manufacturers when receiving cells from storage. Manufacturing organizations should select providers with established record-keeping systems for storage and shipment to combat this type of contamination risk. Specifically, "freezer temperatures should be monitored continuously by a calibrated system…Excursions in temperature should be evaluated using a mean kinetic temperature analysis and documented as a GMP deviation."[4] This emphasis on meticulous record-keeping promotes accountability and traceability throughout the entire supply chain. Complete temperature records maintained from storage through shipping give the client confidence throughout every step in their material's journey that is reinforced with data that provides a record of their cells' viability.

Cryoport Systems developed a unique system that goes beyond record keeping and is unmatched within the life sciences industry. The Chain of Compliance® upholds the strict regulatory standard of ISO 21973 to give our clients complete transparency and control over their material's journey for maximum reliability and peace of mind. This system establishes complete identification of the equipment and processes used in managing the environmental control of the commodity throughout the supply chain, including:

1. Identification of equipment performance
2. Requalification history
3. Commodity history
4. Courier handling and performance history
5. Calibration history
6. Correlation competencies

By leveraging extensive data collection and management capabilities, the Chain of Compliance® implements preventative measures that can ensure the safe delivery of invaluable materials while actively mitigating risk throughout the entire supply chain. Our clients gain the ability to see inside the entire transport process from storage to facility no matter how far the material will travel.

Cryoport Systems' focus on risk mitigation and compliant procedures provides the support required to decentralize and store master cell banks at all temperatures and term durations through a network of global GSCCs. By adhering to compliance standards and established best practices, our solutions meet the risk management demands of the cell and gene manufacturers that trust us with their cell banks. Contact our team for more information regarding our cell and gene supply chain support solutions.

Resources & Further Reading:

1. Byer, H., Wang, W., & Mogilyanskiy, L. (2015, July 31). Mastering Cell Bank Production. BioPharm International. https://www.biopharminternational.com/view/mastering-cell-bank-production
2. *Guidance for Industry: Characterization and qualification of cell substrates and other biological materials used in the production of viral vaccines for infectious disease indications*. (2010, February). FDA. https://www.fda.gov/media/78428/download
3. Part 211 – Current Good Manufacturing Practice for Finished Pharmaceuticals. (2024, July). eCFR. https://www.ecfr.gov/current/title-21/chapter-I/subchapter-C/part-211
4. Montgomery, S. A., Wheelwright, S., & Poon, H. F. (2021, June). Contractor Perspectives: Best practices for transfer, handling, testing, and storage of cell banks. https://www.bioprocessintl.com/cell-line-development/contractor-perspectives-best-practices-for-transfer-handling-testing-and-storage-of-cell-banks