Selecting Your Off-site GMP BioPharma Storage Provider

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Abstract

Off-site storage of GMP biological and pharmaceutical products and medical devices is a critical resource for biopharmaceutical companies, contract manufacturing organizations ("CMOs"), and contract development and manufacturing organizations ("CDMOs") facing storage and overflow issues. There are many critical factors to consider when selecting an off-site GMP storage provider. Among the most crucial factors to consider:

1. Physical site security and accessibility
2. Facility and equipment integrity
3. Precise temperature monitoring and climate control
4. Product safety and inventory control
5. Compliance procedures

Introduction

The safe and proper storage of biopharma product is vital in the pharmaceutical manufacturing industry. As the demand for CDMOs to fulfill production increases, the demand for increased storage capabilities grows. CDMOs are susceptible to storage related bottlenecks primarily before and after the manufacturing process. A delay in customers taking delivery of finished products combined with insufficient on-site storage capacity can lead to an overflow. In other cases, manufacturers desire to increase their US based inventory of APIs and other materials to mitigate the risk of international supply chain disruption. Common overflow materials can include finished product, active pharmaceutical ingredients ("APIs"), large-volume raw materials/chemicals, and medical supplies/devices.

As companies look for off-site GMP storage, there are a number of critical factors that must be considered to ensure that product safety, integrity and accessibility are maintained.

Figure 1. 24/7 video surveillance and fire suppression systems are just two components of critical infrastructure necessary for a well-designed GMP storage facility.

Physical Site Security and Accessibility

Access Controls - The storage facility must be equipped with multi-level access controls throughout the site. The storage provider must have Standard Operating Procedures ("SOPs") in place that detail these controls and access requirements.

Facility Access - The most prevalent approach to establish these controls is via scan badge access. Company employees are issued an individual badge to allow access into and around the facility.

Departmental Access - Access to product storage and operational areas are restricted to authorized personnel only and are further protected by entry doors requiring scan badge access.

Product Access - Entry measures are required in areas and chambers where product is stored (i.e. physical or electronic locking mechanisms) so that only authorized personnel can access customer products.

Video Surveillance, Security and Fire Suppression - 24/7 high resolution video monitoring at all facility and product storage entry points provides visibility into the movement of product and personnel through the facility. This data must be stored and saved.

Fire suppression and a security alarm monitoring system must be in place to ensure personnel, facility and product safety. The alarm monitoring system must alert designated on-call staff in the event of alarm activation.

Facility and Equipment Integrity

Facility Power – Redundant backup generator with an automatic transfer switch is essential. If the facility loses power the generator must be able to keep the facility operational for a minimum of 72 hours while the power situation is addressed. As a best practice, a second generator system and additional transfer switch should be in place to ensure power continuity in the event that the first generator experiences operational issues. The generators must be subject to a preventive maintenance schedule. Agreements with local fuel suppliers must be in place for emergency re-fuel considerations.

Chamber Redundancies – Redundancies for reach-in Controlled Temperature Units ("CTUs") are typically spare chambers. Backup chambers must be ready to be activated in an emergency by being in a calibrated and validated state. It is not feasible to have a backup walk-in chamber. Walk-in redundancy must utilize the chamber infrastructure such as dual primary redundant refrigeration systems to ensure that in the event of unforeseen mechanical issues the CTU can maintain the required temperature range. These systems should run alternately to ensure maximum effectiveness and efficiency and to ensure that both systems are properly operating. It is a best practice to implement additional redundancies from an alternative back up source such as a liquid nitrogen supply for cold-chain CTUs.

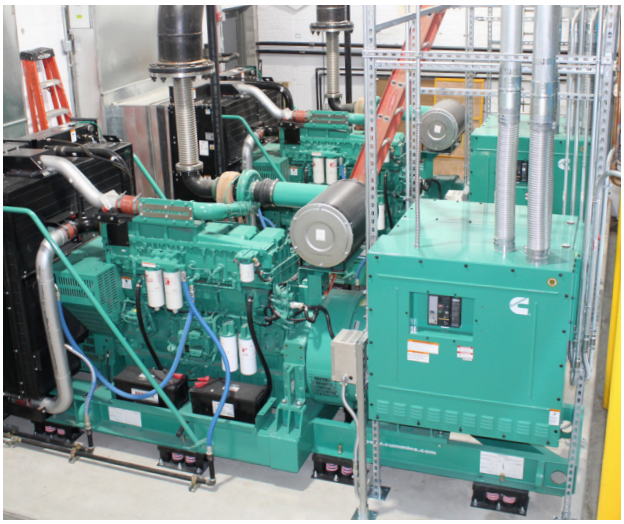

Figure 2. Redundant generators ensure that storage temperatures are maintained in the event of grid power loss due to storms or other unplanned events.

Precise Temperature Monitoring and Climate Control

CTU Monitoring – Each CTU must be equipped with a precise calibrated and validated temperature monitoring system. This system must continuously monitor chamber conditions (i.e., temperature, as well as RH, if applicable). It is imperative that the monitoring system has an alert notification system in which designated personnel are contacted in the event that chamber conditions exceed the operating range. An advanced aspect in the monitoring of chamber conditions is the concept of early warning alarms. These alarms alert personnel to a variation in the normal temperature trends which indicate temperature is moving up or down, heading to an out-of-tolerance condition in the chamber. Early warnings provide the operations group with sufficient time to address problems before they lead to an excursion event.

Predictive Monitoring – Predictive Monitoring Units ("PMUs") track and record performance markers on the mechanical systems of each CTU. A PMU system tracks performance trends for drifts in compressor function, erratic solenoid activation, and liquid component performance to identify and address potential mechanical issues prior to their failure. This allows for potential issues to be noticed months before a catastrophic failure prior to affecting the environment inside the chamber itself.

Figure 3. Monitoring systems must be calibrated and provide excursion alarms. Ideal systems take this a step further with predictive monitoring capabilities.

RH Control - To prevent mold and mildew contamination, which would be a catastrophic occurrence, warehouses and cold rooms should utilize air dryers to reduce the humidity level.

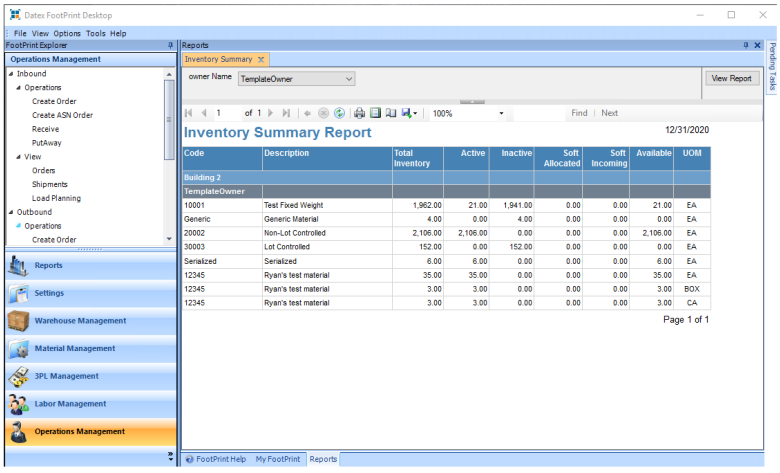

Figure 4. A validated inventory control system tracks the physical location of stored customer items at all times, preventing loss or damage.

Inventory Control and Product Safety

Inventory Control System– A validated inventory system tracks product identification information as well as the storage chamber and location of incoming products. An inventory system tracks the whereabouts of all products in storage with respect to temperature condition, quantity, and physical location throughout the life cycle while at the storage provider.

Product Safety – Loading docks equipped with a leveling system allow for the safe and proper loading and unloading of delivery vehicles of all sizes into the facility. Product storage areas must be clearly defined with location identifiers to allow personnel to quickly identify where product is placed during the shipping and receiving processes. The storage areas should be organized in a manner in which personnel, product, and operational equipment (hand trucks, forklifts, transportation carts, etc.) can travel safely and directionally without limitation.

Hazardous Material Control - The off-site storage provider must have an established hazardous material control program that details the acceptance criteria, hazard classification and/or Biosafety Level ("BSL"), storage and volume requirements, and handling and disposal procedures for products that are considered hazardous material.

Special attention must be paid to the controls in place in regards to storage and segregation of flammable materials. The off-site storage provider must have a mechanism for employees to access the Safety Data Sheets ("SDS") of products stored in the event of an emergency.

Compliance Procedures

Quality Management System ("QMS")
An established and effective QMS ensures that company initiatives and policies meet customer and regulatory requirements. The quality department provides oversight of the GMP processes, company training program, investigations and corrective actions, and document control. A structured system of company policies, operating procedures, and work instructions ensures continuity and compliance throughout the organization and establishes confidence in both customers and employees alike.

Validation
Ensuring that CTUs, temperature monitoring systems, and inventory systems are operating as expected must be proven and verified through the process of validation. The off-site storage provider's Site Validation Master Plan details the plans in place to ensure that all validation activities are performed in a manner that satisfies regulatory and quality compliance requirements. For more information on the importance of thermal mapping and validation reference Alex Debreceni's white paper entitled **"Planning a Successful Warehouse Mapping Study."**

Figure 5. IQ/OQ/PQ validation must be performed when a GMP storage facility is first commissioned, followed by appropriate requalification intervals.

Conclusion

An off-site GMP storage provider is a valuable resource for keeping CDMO production lines moving by providing timely additional storage capacity and flexibility.

When evaluating off-site GMP storage facilities, take the time to learn about the provider's redundancies, monitoring system, physical security, product handling processes and QMS compliance.

Selecting a storage provider to keep your valuable retains, samples, products and overflow items is an investment. Thorough research will pay dividends as you sleep at night knowing your precious items are safe, under lock and key, and continuously monitored.

While there are a number of additional considerations involved in the selection process, physical site security, redundancies, temperature monitoring, product safety, inventory control and quality compliance are the most important.

A reputable storage provider will welcome your questions and provide the answers you need as your valued partner.