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Requirements for Outsourced Cold Chain Logistics and Storage in BioPharma Development

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Between 1999 and 2003, the pharmaceutical market experienced an aggressive compound annual growth rate of 11%. During that same timeframe, the biopharmaceutical market grew at nearly twice that rate, or 21%.[1] This market segment, which was responsible for $41 billion (10%) of pharmaceutical product sales in 2003, has expanded rapidly for many reasons such as the greater potential for these products to *cure* diseases, not just treat symptoms, their highly effective nature and their tendency to cause fewer side effects.[2]

However, because these biologic molecules are generally larger and more fragile than their pharmaceutical counterparts and are more sensitive to temperature fluctuations, these products pose new storage and handling challenges that lead to increased costs for manufacturers. The challenge of preserving quality and efficacy under these conditions has also led to new governmental requirements and regulations for storage and handling and has caused the industry to reevaluate the existing pharmaceutical supply chain model.

As this change has been occurring, all biopharma firms, from small drug discovery firms to large integrated biotech organizations, have been increasingly focused on controlling costs and maximizing operational efficiencies to sustain growth. This emphasis is bringing about a shift from the traditional in-house storage and logistics model to an outsourced one, because contracting out these services to specialists helps manufacturers streamline their supply chains, keep operating costs in check, reduce time-to-market and focus their resources on core competencies such as research and development.[3]

Given the changes occurring in the marketplace (new handling requirements, governmental regulations and the evolving supply chain process), finding a qualified partner that offers outsourced cold chain logistics and storage services can be a difficult undertaking. Some key considerations that should drive this search include the potential partner's:

1. Supply Chain Evolution
2. Regulatory Compliance
3. Technological Innovations

Supply Chain Evolution

The new demands that biopharma products place on the supply chain are driving changes to the traditional shipping, storage, packaging, tracking and business processes that the average supply chain can't handle. These demands often require manufacturers to develop specialized in-house cold chain logistics facilities, systems and processes or outsource these functions to specialists. The pharmaceutical supply chain has begun to refocus after many years of little change and the movement to outsourcing has been growing at a steady pace.

One of the most important considerations when making a decision to outsource is whether the potential partner has evolved with the changing needs of the market. A potential partner should have: cold chain management expertise, impeccable quality and customer service standards, advanced processes and customer conveniences and specialized cold storage facilities.

Cold Chain Management Expertise: *The Journal of Commerce* estimates that temperature-sensitive shipping is growing at a rate of 15% per year, and temperature-controlled products make up 13% to 15% of the air-cargo industry, the largest single category of airborne goods.[4] Although biopharmaceutical products represent just a portion of this market, they represent one the largest growth areas for the air freight business.

Five to ten years ago "cold chain management" was still a buzzword in the industry and only a few companies were focused on this effort. The industry realized that shipping temperature-sensitive products was a unique problem because temperature could be affected by many factors (such as the carrier, the route and delivery times). This created the need to control thermal variability throughout the supply chain.[5] Now, this process—cold chain management—is a burgeoning industry: there are monthly seminars on the subject led by experts in the field and new companies, associations and trade organizations that solely serve this niche:

The Pharmaceutical Cold Chain Discussion Group (PCCDG), a section of the Parenteral Drug Association (PDA), has worked extensively

to develop a guideline that defines best practices in cold chain management. PCCDG's Technical Report No. 39 (Cold Chain Guidance for Medicinal Products: Maintaining the Quality of Temperature-Sensitive Medicinal Products through the Transportation Environment) which was released in 2005 provides strategic direction on developing processes for handling and transporting such products.

Dedicated contract services are offered by specialized, outsourcing cold-chain logistics and storage providers for biopharmaceutical products.

The air transportation industry has created **The Cool Chain Association,** which estimates that 30% of all perishable shipments are lost in transit. The association has developed recommendations for maintaining and standardizing the handling of these products to help minimize loss.[4] These guidelines will be similar to the International Air Transport Association (IATA) guidelines for the hazardous materials.

Impeccable Quality & Service Standards: A contract cold storage and logistics partner must, above all, be committed to excellence in quality control and customer service. As an extension of the biopharmaceutical manufacturer's business, the contract service provider must operate as a committed stakeholder to protect product integrity as well as the manufacturer's business viability and reputation in the marketplace.

Measures of excellence in the supply chain include:

- Skilled, dedicated quality assurance and operations teams
- Well-documented standard operating procedures (SOPs)
- Adherence to all applicable regulations and guidelines
- State-of-the-art, secure cold storage facilities and technologies
- A singular focus that allows contract service providers to be experts in their niche areas[6].

Advanced Processes & Conveniences: The traditional supply chain model is built on deploying inventory to a network of national distributors, where products often await shipment for long periods of time. The emerging, more-efficient model is based on a smaller regional network of a few highly-specialized third-party logistics (3PL) and cold storage providers that can receive and ship a larger volume of inventory on a "just-in-time" basis, enabling greater efficiency, economies-of-scale and workforce flexibility.[3]

This model also enables "shared-user logistics" wherein the service provider spreads infrastructure, administration and overhead costs among its clients, providing each client with significant cost savings. The end result for manufacturers is reduced time-to-market and new supply chain efficiencies.[3]

When selecting a contract cold storage and logistics provider, manufacturers should ensure that potential vendor partners have well-established systems, processes and distribution partnerships that enable an efficient and effective supply chain.

Specialized Cold Storage Facilities: Generally, pharmaceutical compounds remain stable under a broad range of temperature conditions such as +2°C to +8°C, -10°C to -25°C or even at ambient temperature (between +15°C to +30°C). Many biologic products, on the other hand, must be maintained within even tighter tolerances in cold (+1°C to +5°C), frozen (-30°C or -40°C) and even cryogenic storage (<-160°C). Most traditional supply chain storage processes and systems are not designed to accommodate these conditions.

Developing facilities that can maintain product integrity during packaging, shipping and storage under these highly specialized conditions requires significant capital investments in cold storage facilities, temperature monitoring equipment and shipping containers. Along with these physical assets, hiring trained personnel who understand the impact of biopharma products on the supply chain is vital.

Regulatory Compliance

Regulatory compliance was a simple task in supply chain processes in the past. Good Manufacturing Practices (21 CFR parts 210 and 211) are very limited in their definitions of handling materials. Industry standards have increased in just the last few years and reputable contract cold chain storage and logistics firms must be current on all applicable regulations and must demonstrate full compliance. Topping the list are anti-counterfeiting controls and recently published guidelines from a variety of regulatory bodies.

For example, some of the guidelines delineating best practices and regulations for the industry include:

- The **Food and Drug Administration** (FDA), which issued the FDA 483 Citations for weakness in these areas[1]
- The **United States Pharmacopeia's** (USP) general chapter <1079>, which outlines basic rules for Good Storage Practice and Good Shipping Practices for all pharmacopeial products[7]
- The **World Health Organization** (WHO), which released a new version of the Good Distribution Practices specifically to address the special requirements of this market segment
- The **Health Canada** Health Products and Food Branch Inspectorate Guide-0069, which lists the guidelines for temperature control of drug products during storage and transportation within the Canadian marketplace[8]

Counterfeit drug production has become an international epidemic and is another critical driving force behind increased control and regulation in the biopharmaceutical supply chain. The Center for Medicines in the Public Interest estimates that "counterfeit drug sales will reach $75 billion in 2010, a shocking 92% increase from 2005".[9]

The FDA's Counterfeit Drug Task Force recently announced steps to guard against this growing risk. The measures include regulatory guidelines and recommended technologies that can help safeguard the integrity of the U.S. drug supply.[10] Biopharmaceutical manufacturers must ensure that all contract supply chain service providers comply with all applicable regulations and are committed to the

highest standards of accountability, security and integrity. The FDA guidelines focus on areas such as.[10]

Chain of Custody: By 2007, the FDA will fully implement regulations related to the Prescription Drug Marketing Act of 1987, which requires drug distributors to document the chain of custody of drug products (the "pedigree") throughout supply chain and distribution systems.

Technology: The FDA has identified specific technologies that could be instrumental in tracking pharmaceuticals from manufacturing to dispensation. These include radio frequency identification (RFID) tagging of products with unique serial numbers, color-shifting inks, holograms, and chemical markers incorporated into drugs or labels.

Secure Business Practices: The FDA also recommends that all participants in the supply chain, from manufacturers to shipping companies, warehouse/storage facilities and distributors, adopt secure business practices and only do business with reputable companies.

Technological Innovation

To support the new just-in-time supply chain model, changing regulations and the need for biopharmaceutical developers and manufacturers to maintain visibility into their inventories at all times, the ideal 3PL partner should offer innovative product tracking and management technologies. These systems can take the form of real-time, Web-based inventory management software that can help manufacturers:

Guarantee Product Integrity: By tracking products through all stages of the supply chain and incorporating chain-of-custody details and temperature data with product tracking information, manufacturers gain auditable records showing that their temperature-sensitive products are secure, genuine and uncompromised.

Reduce Cycle Times: Real-time, Internet-based tracking systems that allow manufacturers to access their inventory and schedule just-in-time shipments help reduce cycle times and create efficiencies in the supply chain.

Improve Visibility & Facilitate Planning Cycles: Successful **technology** solutions create a window to manufacturers' product inventories that help them operate with minimal inventory, prevent stock-outs and better manage and plan both production and distribution.

Increase Thermal Shelf Life: The ability to track the complete time during which a product is out of its optimum temperature range can actually allow a manufacturer to increase the potential product shelf life.[11] This provides the manufacturer with real data to make more educated decisions about the viability of products.

Choose Wisely

Although partnering with contract cold chain storage and logistics providers is an increasingly cost-effective and efficient model for handling and distributing biopharmaceutical products, manufacturers are ultimately responsible for maintaining the efficacy, authenticity and quality of their products. It is critical that they partner with a qualified contract chain logistics and storage expert that can help them navigate this rapidly evolving landscape. A successful partnership will help manufacturers ensure compliance; align their distribution models and business processes to develop more efficient supply chain processes; and protect their biopharmaceutical products, their reputations and potential revenues. Understanding what to require in a partner is vital to developing a strong relationship that will support your company's business strategy.[12] ▪

About the Author

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