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Planning for Your Cold Chain Shipment: *The Forgotten Science of Clinical Research and Development*

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Many precautions are taken in a typical research lab to ensure the integrity of biological specimens. Temperature, storage, and personnel access, among others, are all tightly controlled, and codified into standard operating procedures (SOPs), if not almost biblical law. And no wonder — companies have millions invested in biotech solutions whose progress is often measured in years and decades. Scientists have their life's work on the line. So, it is with some surprise that the diligence most companies exercise during the research and development process is not always maintained during specimen transport. Every time a specimen leaves the lab, be it for further analytical testing or investigational purposes, it runs a heightened risk of contamination, especially from fluctuating temperatures. Ensuring that this does not happen should be the responsibility and concern of everyone with a stake in a biological product's success.

There are a number of factors requiring careful consideration when planning to transport temperature-critical shipments. Whether shipping within the United States or internationally, companies run the risk of experiencing costly temperature fluctuations if the numerous components of shipping frozen or refrigerated materials are overlooked.

The safe transport of research shipments such as refrigerated drugs or vaccines, and frozen patient samples or research compounds is accomplished



through coordinated efforts between many individuals. As mentioned earlier, most companies take great care in maintaining an appropriate environment within their operations as well as ensuring that the facilities they are shipping to have the proper storage facilities to maintain temperature integrity after delivery. The challenge lies in the interim transport when most errors spring from a lack of shipment planning rather than a lack of concern.

Can you be sure that a research shipment will arrive at its destination safe and sound? Well, there are no guarantees in shipping, but the following steps can certainly improve the odds.

Packaging Selection

First, let's look at packaging selection. There are many quality packaging vendors that service the needs of the pharmaceutical/biotech community. Most of these companies market qualified packaging systems that will maintain frozen (-78°C) or refrigerated ($2\text{--}8^{\circ}\text{C}$) temperatures for 24 hours and

beyond. The term "qualified" refers to the testing that is conducted on a packaging system to ensure that it maintains a certain temperature. However, certain materials have unique packaging needs that warrant a more customized packaging solution. In these cases, it's worth considering having your packaging system qualified to verify its performance under the rigors of a door-to-door shipment. Shipments can be exposed to a variety of temperature extremes, especially when dealing with global transportation. For example, winter shipping from the eastern United States to Australia, where it is summer, will expose a shipment to a wide range of temperature variations. Will your packaging system perform under these conditions?

Most packaging companies have laboratory testing facilities to replicate various conditions such as heat, cold, and humidity. Making clear to the packaging company how the box will be used and where it will be shipped will assist them in performance testing.

Following selection of a packaging

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system, choose a temperature monitoring device that will measure the internal temperature of the packaging system during the time the product will be inside the box. Be certain to understand proper placement of the devices to minimize false readings, which sometimes occur if probes are placed too close to frozen gel packs.

Communications with the Transportation Vendor

The next and most important step in the cold chain shipping process is communications with the transportation vendor, who should be brought into the planning process as early as possible.

Several factors influence transportation company shipping decisions. The first is "lane segment" selection, which refers to the destination city and country for transported goods. There may be flight limitations and lengthy import permit application processes that can extend transit times. However, transit duration can be reduced by establishing pick-up times that coincide with freight lodgment and flight departure times. Size and weight of the shipment can also be a factor if you are moving large quantities of temperature-controlled material.

The best method for communicating with a transportation vendor, especially for large ongoing clinical trial projects, is to develop an SOP. This document should contain information on the selected packaging system and contain answers to crucial questions such as:

How long will the qualified packaging system hold the desired temperature?

Who does the transportation company contact in the event of unforeseen delays?

What are the delivery acceptance hours of the recipient?

Can the receiving location receive material after hours?

Will the transportation vendor clear the shipment through customs, or

must they work through the recipient's pre-arranged custom brokerage arrangements?

All of this information is necessary to ensure that a cold chain shipment arrives at its destination in a timely, uncompromised condition.

These seemingly minute and tedious details allow a transportation vendor to select the optimal routings to all the destination points as well as enable more effective communication with airline partners. Developing these SOPs up front also ensures that any communications with third-party customs brokers take place well before the first shipment is collected from the facility. If there are delays or unforeseen customs issues, the vendor will have already provided instructions on proper storage of the shipment and how to maintain the temperature until the issue is resolved.

Finding the Right Vendor

It is important to select a transportation vendor that understands your business and the unique challenges that frozen and refrigerated shipments pose. Most premium courier services or freight forwarders work with commercial airlines, allowing greater flight selection and scheduling flexibility. Some airlines actively seek the business of those with cold chain transport needs by touting their specialized personnel training and value-added SOPs to provide proper handling of shipments within their system. The transportation vendor should know who these carriers are and should endeavor to work within their networks.

In addition to integrating with air carrier networks to keep customers abreast of real time status, vendors should be able to provide their own online services including, but not limited to web-based export documentation creation and electronic tracking.

Airlines that market cold chain products will sometimes give preferential treatment to pharmaceutical products. Their infrastructure and processes have been validated both internally and externally, and they recognize that temperature variances on an aircraft can

The Four Fundamentals of Cold Chain Shipping

1. PACKAGING

Package must be qualified to ensure that it can maintain the correct refrigerated or frozen temperature range.

Shipping schedules and destinations play a major role in package choice.

2. COMMUNICATION

Transportation vendor(s) should be brought into the planning process as early as possible.

Standard practices should be codified to determine lines of communication.

The more information provided about the nature of the shipment, the easier it will be for an optimal route to be determined.

3. THE RIGHT VENDOR

A vendor should have established relationships with commercial airlines specializing in cold chain shipping.

Premium courier services offer more flexibility and control.

A vendor should have the technical ability to link with airlines for real time status, generate web-based export documentation and provide electronic tracking.

4. DOCUMENTATION

International shipping requires extra diligence due to varying import and export regulations between countries.

Documentation should always be in order before beginning shipping.

Documentation should always explain the purpose of the shipment (*i.e.*, research, investigational purposes) to guarantee clear communication with customs.

impact the goods they are transporting. These airlines have proper storage facilities, preferred loading positions, cockpit notifications, checklists, and expedited ground handling to minimize the risk of exposing shipments to the elements.

Most companies that transport frozen and refrigerated shipments tend to ship Monday–Wednesday to avoid heavily trafficked weekends. This makes it less likely that your shipment will be removed from a scheduled flight due to loading or density issues. Early weekday shipping also helps reduce the risk of shipments being held in an environment where optimal temperatures cannot be maintained.

There are also premium service courier companies that specialize in handling temperature-controlled shipments with 24/7/365 coverage. These companies can ensure that dry ice is replenished for frozen shipments and that refrigerated shipments are maintained in refrigeration. Because these companies do not consolidate shipments with cargo from other customers, they can offer a greater degree of control and communication.

Documentation, Documentation

Paperwork for customs purposes must be in order before shipping internationally. You should be able to ascertain what export and import documentation is required by working closely with your logistics departments or transportation provider. Customs delays can and do happen due to inaccurate or incomplete customs paperwork.

Basic guidelines for creating a commercial invoice should be followed to ensure the proper verbiage, number of copies, etc. If something is being transported for research or investigational purposes, note that fact as part of the reason for shipping.

For international shipping, investigate whether the commodity requires import permits. The application process can be lengthy in some countries for these permits. When conducting an overseas clinical trial, a permit is required to import your study drug. This is separate from the permit that may be required to export patient specimens.

As stated previously, if the recipient has nominated their own customs broker, provide those details to the transportation company to clarify responsibilities. Make certain that customs valuations are reasonable and also understand who will pay duty and value-added tax on the import. To avoid delays, sufficient funds should be available to pay these taxes.

Unforeseen circumstances may surface during the cold chain shipping pro-

cess. There are an endless number of variables that must be accounted for and not all of them can be controlled. But risk can be mitigated by taking the time to plan a shipping program with the same care that is put into the research process. Cold chain shipping is but a small part of clinical development, but the headaches averted by correct management of this endeavor are well worth the added time and investment.



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