Cold chain logistics

Need of the hour

Supply chain demands specialised handling for sensitive goods, like certain temperature-sensitive drugs, during transportation, irrespective of the transit route taken. Also, ensuring the arrival of sensitive goods in a usable condition calls for the use of cold chain during transport. This article delves into the various challenges encountered in this area and ways to overcome them.

Jayanti Vaidyanath

Clinical trials are becoming increasingly complex, as biopharmaceutical companies respond to growing concerns over the cost and safety of new drugs. Clinical studies have moved beyond primary cities and towards more remote investigator site locations. Components of a clinical trial often occur in different countries, which follow their own regulations for the clinical trial process. There is a growing awareness on the importance of cold chain requirements for temperature-sensitive pharmaceutical products. Sponsors and Clinical Research Organisations (CRO) alike have realised the need to focus on the investigational products that are being distributed, stored & handled at right temperatures along with the traceability to prove this maintenance. These complexities have resulted in a significant shift in the balance of power towards clinical supply chain specialists.

For the industry, four per cent of the cold chain shipments en route the destination experience temperature fluctuations (commonly called 'shipping excursion') that makes the supplies unusable, even if temporarily. A shipping excursion is a negative event that occurs during shipping, wherein the product exceeds its specified temperature limits. Stability data on the product on investigation will result in a release or destruction of the excursion product. On an average, about 2-4 per cent of the cold chain supplies never arrive in a usable condition. The average cost for shipping excursions can exceed $ 150,000 and commits over 2,300 staff hours for an average cold chain-related study. For a large pharmaceutical company, which may have 15-20 studies per year, such excursions may multiply costs by millions of dollars, as noted by Roy Goff, Pharma Outsourcing.

Growing requirements of cold chain

Today, the global biopharma cold chain market is estimated at $ 5.1 billion, and is expected to grow to $ 6.6 billion by 2011. *Pharmaceutical Commerce* has published *'Cold Chain Biopharma Logistics Sourcebook 2010',* a first ever study of the booming business in temperature-controlled shipping of biopharma products, which assesses the impact of new regulations, new packaging & shipping technologies and the faster-than-average growth of biopharma products that require cold chain shipping. While the North American market is expected to grow by 15 per cent during the 2008-11 period (or about 5 per cent annually, in line with the overall pharma market), the global market will show a growth rate that is double this amount.

Courtesy: SIRO Clinpharm

The study has surveyed growth rates for pharmaceuticals, biotechnology, vaccines, blood products & clinical materials, US & international regulatory bodies like US Food and Drug Administration (FDA), United States Pharmacopeia (USP), Parenteral Drug Association (PDA), International Air Transport Association (IATA), Medicines and

Healthcare products Regulatory Agency (MHRA), etc, as well as air, ground & ocean carrier modes. It also includes packaging materials & technologies, refrigeration systems and instrumentation.

Nick Basta, Editor-in-Chief, *Pharmaceutical Commerce,* and co-author of the report on *Biopharma Logistics,* observes that the global biopharma industry is growing more towards biologics and projects. Seven of the top 10 global pharma products in 2014 will require cold chain handling. Further, while significant attention has been given in the past year towards preparations for the H1N1 flu season, a simultaneous and dramatic growth has been observed in the world vaccine market, both for infectious diseases and other conditions. Various industry sources estimate the vaccine market to grow on an average of 8 per cent per year through the next five years.

Meanwhile, the clinical trials industry, which has been expanding globally in recent years, will add more volumes to this growth in future. Clinical trials materials (CTM) have evolved to the extent where they require specialised logistics market. For example, it has been reported that recently, a single CTM shipment required its own chartered jet to carry 65 metric tonnes of temperature-controlled material, from Europe to the Far East.

Compliance officers and supply chain managers have several options of validated technologies and transportation processes, particularly for real-time monitoring of a shipment's condition, many of which are affordable. All biologics may not necessarily require cold chain handling but trends indicate that even products stored at room temperature will soon require additional monitoring steps, which may thus add complexity to the transportation process.

Monitoring product circulation

Excellent cold chain monitoring & packaging systems maintain the integrity of the pharmaceutical or investigational products during the manufacturing and supply chain processes. Highly efficient & user-friendly monitoring systems automatically & continuously monitor the environmental conditions during handling, storage and transportation of pharmaceutical or investigational products. A number of monitoring solutions like the wired or wireless sensor networks, data loggers and thermocouples effectively monitor manufacturing facilities, warehouses & storage areas, during transportation & shipment.

Shipping, insulation and packaging technologies are now offering better materials such as the inner polystyrene container with Vacuum Insulation Panels (VIP), polyurethane and phase change materials. Reusable temperature-controlled containers are also available for international shipments. Another important tool that helps in land transport is the availability of temperature-controlled trucks.

Challenges & ways to counter them

A number of factors act as impediments for the pharmaceuticals transport management. Of these, cold chain logistics and storage depots face substantial challenges in the way of proper functioning.

Cold chain: The complexity in the transportation process poses new challenges that involve maintaining cold chain during movement of goods to remote locations, more exchange & drop-off points and varying distribution environments, which often involve lengthy clearance procedures at customs end. Moreover, some of the other challenges include various modes of transportation, lack of adequate logistics infrastructure, numerous carriers & couriers, specialty packaging solutions, different climate zones and seasonal changes. Large studies may involve shipment of large volumes of refrigerated patient kits worldwide while maintaining and documenting appropriate temperature conditions.

Temperature excursions during storage, handling or distribution of temperature-sensitive CTM pose significant safety and financial risks.

One way to counter this challenge is to collect the necessary data and information upfront to have a clear understanding and knowledge of the storage & transport conditions, which will prevail throughout the supply chain. The pharmaceutical manufacturer, logistics provider, packaging designer and data logging supplier should together discuss the project to ensure maintaining clarity throughout the process. The storage conditions during shipment may involve encountering uncontrolled environments through various transport operators, during different seasons, several storage warehouses and depots or pharmacies, etc. While pharmaceutical warehouses and storage areas are generally controlled environments with easier validation, uncontrolled environments during the transportation and distribution of drug products by ground, sea or air represent the greatest challenge to sponsors.

Storage depots: CTM storage depots with local presence play a significant role in ensuring proper storage and delivery of Investigational Product (IP) to sites within their country. They have a good understanding of the regulatory requirements, storage conditions, distribution and logistics challenges according to seasonal requirements. It is therefore inevitable that sponsors rely on their experience, expertise & infrastructures and use them as their local depot. This lowers the risk of delays due to the import processes as well.

Storage depots should ensure compliance with cold chain regulations by acting on the following quality aspects of cold chain:

1. Carry out temperature excursion test studies
2. Update their cold chain quality system by ensuring regular revisions of standard operating procedures and personnel training
3. Carry out regular validation of all cold chain processes and equipment by mapping the warehouses & storage areas
4. Carry out dummy shipments to study temperature data during movement of goods to validate the qualification of temperature-controlled transport storage shippers.

Major guidelines to follow

Apart from the regulatory requirements of individual countries, relevant guidelines

are also available to ensure maintaining high levels of security and safety for the drug products throughout the supply chain, from the manufacturing facility up to the final end-users or patients. Some of these major guidelines include Good Laboratory Practices (GLP) for the drug development aspect, Good Manufacturing Practices (GMP) for the manufacturing side, Good Clinical Practices (GCP) for the clinical trial side and Good Storage & Distribution Practices (GSDP) for the pharmaceutical supply chain aspect.

Key risks due to cold chain failure

- Patient could be administered an unsafe product
- Lack of compliance with global regulatory and standards-based requirements can increase liability
- Thermal variability can lead to inconsistent results between and within batches
- Shipment can be rejected by the quality department, leading to costly delays—increasing the complexity of trial management

Courtesy: R H Bishara, Good Cold Chain Management Practices for Clinical Trial Materials, Pacific Region Clinical Supplies (PARCS), San Diego, CA.

Looking forward

Summing up, it can be stated that the aim of conducting a clinical study is to mitigate and ultimately eliminate the bottlenecks so as to deliver the supplies on time and in a condition that satisfies the enrollment or quality needs of the study sites. This activity is for both project and risk management.

According to Goff, certain activities essential for project and risk management include identifying the locations of the sites where the clinical study is to be carried out and identifying any special requirements for logistics planning at sites, eg, narrow corridors that cannot allow passage of a pallet, winding staircases, small refrigerators, etc. One should track the study transportation routes from the distribution location to clinical trial site and look at the likely temperature variation situations that may occur en route. Another important step to consider is calculating the duration, date or time for the movement of supplies to ensure that delivery does not occur on a holiday, ie, when the site is closed. Temperature range or duration of shipments needs to be verified against shipping container specifications to determine any special shipping container design needs. Verification processes should be carried out so as to avoid leaving out any specialised cold chain activities. People involved in this activity should work with partners in order to seek feedback from sites, couriers, freight forwarders, CROs and contract manufacturers to obtain the optimum approach for the study, country & site.

Jayanti Vaidyanath is Vice President Administration, Legal and Clinical Trials Supplies Management at SIRO Clinpharm.

For further details contact Corporate Communications-Head: Aniruddh Patwardhan, email: aniruddh.patwardhan@siroclinpharm.com