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Temperature Excursion Management in Cold Supply Chain of Pharmaceutical Products

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Abstract

India's cold chain industry is currently estimated to be worth $8 million which is composed of a combination of refrigerated transportation and surface storage mechanism. Managing the quality of pharmaceutical product during cold supply chain and the distribution process is a complex challenges for the pharmaceutical industry. The Indian cold chain market is anticipated to be more organized in setting up the cold chain facilities across India in coming years. The temperature should be maintained for the storage and transportation of temperature sensitive goods during the entire product life cycle right from the receipt of raw material and its manufacturing till distribution. There is a need of special handling and monitoring of the refrigerated product to ensure the proper packaging configuration and transit methods meet the predetermined cold chain criteria. Improper handling might deteriorate the quality of the product thereby lowering the therapeutic properties. The study focuses on a system based quality management in pharmaceutical operations, quality assurance and enhancement, concerted efforts, concepts, consequences and handling mechanism to ensure product quality.

Keywords; *Temperature excursion, distribution, pharmaceutical products, transportation.*

INTRODUCTION

A cold chain can be defined as distribution and supply of those therauepetic drugs which are stored under specific temperature range. The product stored are those that undergo end to end transit to transport a sensitive product like pharmaceutical drugs and biologics materials. The proper maintenance, control and handling of such products is extremely important in pharmaceutical manufacturing and distribution. A cold chain maintains and preserves the usability of products, mainly pharmaceutical products which require constant refrigeration. Certain other biosimilar, therapeutic drugs also come under the ambit of cold chain. The cold supply chain distribution method also focusses on not only the packaging of insulated containers having appropriate quantity of refrigerant but also on the transportation and storage handling of the drug product. All the essential elements should be properly analyzed, understood and tested before the distribution process is carried on. This will ensure that the quality of the product and patient safety is not compromised.

The human negligence and the improper management of the environmental controlled parameter during storage and handling impact the quality of the drugs distributed. Such uncalled and uncontrolled situations call for lower efficacy and deteriorated drug quality resulting temperature excursion. Failures to store the medicines as per the set standards of manufacturer can invalidate the safety of medicines which are stored in large quantities and are temperature liable. This can cause an unavoidable waste to a large expense.

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Objective: The study focuses to find out the various facets of temperature excursion in the transportation and distribution in cold supply chain of pharmaceutical drugs.

Methodology: The paper is based on the secondary database and exploratory study through various articles, journals and news portals.

Facets of Temperature excursion : The pharmaceutical cold chain and managing transportation of temperature controlled products is one of the major complex challenge. Continuous growth has been observed in the temperature controlled products indicating tremendous growth globally. With the introduction of Goods Distribution Practices (GDP's) there has been clear demarcation for the storage of biologics and other products at a definite temperature. Use of refrigerants, insulated containers and temperature monitoring electronics are some logistics practices employed to monitor products when shipped. The pharma manufactures still follow the traditional practices of analyzing the environmental conditions and documenting the temperature stability of their product. But because of the safety regulators guidelines to be strictly adhered the pharma manufactures are now focusing to provide better quality assurance.

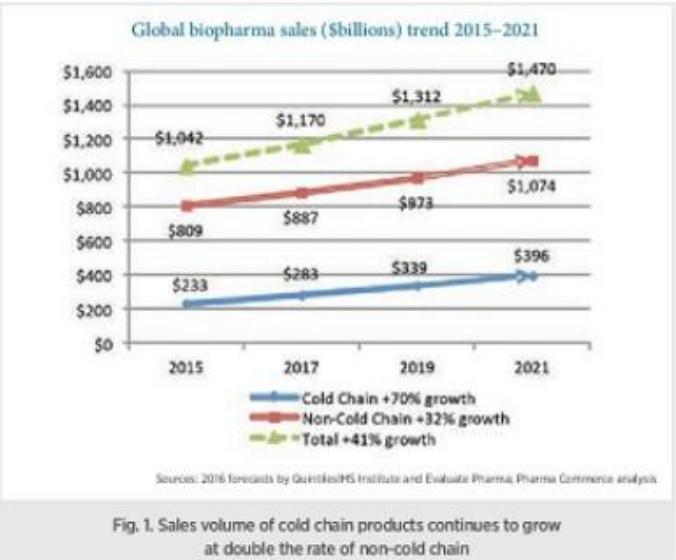

Fig. 1. Sales volume of cold chain products continues to grow at double the rate of non-cold chain

a. Handling temperature excursion:

The pharmaceutical manufactures dealing with the sensitive products having shorter shelf life, greater sensitivity needs to maintain the specified range of temperature to avoid the uncontrolled situations. If temperature range exceeds from the specified range the product experiences temperature excursion. If so is the case then the manufacturer should immediately follow the rules shown below and quick action should be taken to prevent the waste.

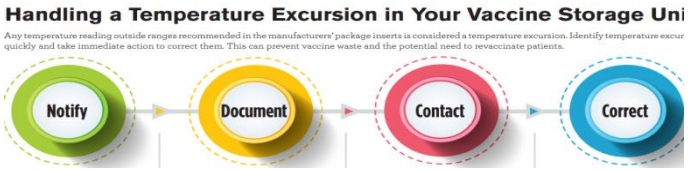

Fig: 2 Source :US Department of health and Human Sciences

The products which are temperature sensitive can deteriorate the active ingredients and decrease the content through transformation of degraded components by receiving thermal energy. The uncontrolled storage and distribution temperatures of the drug may lead to harmful side effect when administered by the customer.

b. Stability of pharmaceutical preparation:

The stability testing during pharmaceutical preparation is carried out to provide an evidence on the quality of drug substance over a time period where the identity, strength, quality and purity of the drug is not affected. The quality of drug varies with time under changing environmental factors and so the shelf life of the product is studied during stability testing .The manufacturer must provide the information on real time stability studies, chemical and microbial attributes along with the expiry date and storage condition which were previously projected. Within the specified limit of shelf life, lifesaving drug must possess the ability of retaining its physical, chemical therauepetic properties. Following the proper current regularity guidelines and understanding the changing climatic zones drug stability information should be sought, collected and

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analyzed thereby preserving its microbiological attributes.

c. Storage conditions and limitations:

For a pharmaceutical drug the shelf life always relates to its storage conditions along with its compliance with labelling. There are various types of storage conditions which are required for pharmaceutical drugs. The drug substances are stored in different required conditions and temperatures are set standards by manufacturers. There are certain specific chemicals and solutions which are required to be stored in specific conditions only. So, most of the drug substance experimental studies on storage conditions are performed at room temperature. 20 -25 C temperature is considered room temperature for pharmaceutical drugs. The excipients and APIs are stored under the controlled temperature. The 8 to 15 C temperature maintenance in the warehouses is known as the cold storage conditions. Some substances which are likely to degrade at room temperature are stored at specified storage condition maintaining the efficacy of the drugs. The storage conditions needs to be precisely indicated as a label:

-The drug substance to be stored under normal storage condition.

-The drug substances to be stored between 2 and 8 0C (under refrigeration, no freezing).

-Storage below 8 0C (under refrigeration).

- Storing the product/substance between -5 and -200 C (in a freezer).

-Store the product/substance below -18 0C (in a deep freezer).

2. Reasons for temperature excursion:

Temperature monitoring at every phase during cold supply, not only in manufacturing stage but also at all stages of storage and transport which is of utmost importance for the products which are temperature sensitive. The products which are exposed to higher temperature or moisture levels are prone to lose its efficacy. The integrity of cold chain is threatened during transportation by many risks, not limited to natural disasters, handovers and unforeseen delays. The EU GDP guideline explains that the drugs are expected to be held at right condition at all time throughout storage and transport. The quality needs to be ensured at all stages by the manufacturer and distributor. The inadequate air handling unit (AHU) are required to maintain the specific temperature, rupture of air duct, breakdown of power failure, insufficient cooling effect, the unexpected delay of transportation, environmental conditions, product if kept on heating zones of airports or yards also defunct the efficacy of the products and are also some reasons for temperature excursion.

3.Transportation of cold supply chain products:

The lifesaving medication when transporting is arguably more important than manufacturing them. Shipping these products require extra level of care. Precautions are necessary like temperature control, environmental conditions and safeguarding drugs against adulteration. Many pharmaceuticals especially, controlled substances are highly covered because mismanagement can cause counterfeiting of drugs. The required temperature must be maintained for pharmaceutical safety and efficacy. The method and the time of transportation, the local seasonal temperature, size and control requirement of the loads should all be considered while the distribution of the cold supply products. For vehicles of little volumes of virus chain products protected compartment with ice packs must be utilized. Damaged products while freezing must not come in direct contact with these ice packs. Therefore the containers should have separate compartment. Transporting and distribution should be continuously monitored using data logging system. The data recording of temperature maintained is retrieved through these data logging devices shipped with the packed product. The thermostatic

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temperature on the transport vehicle should be set on specific requirement for recording and time to time tracking. The recorded data should be available for review. For larger volume of good to be supplied must be shipped with refrigerated transport system, specifically when the transit may prolong.

4. Controlled Temperature Storage:

The temperature controlled logistics specializes in storage, preservation and transportation of those products which are sensitive to atmospheric conditions and needs to be maintained at certain temperature. This is imperative for many pharmaceutical products as the spoiled dugs can have serious consequences on health. The elevated temperature can affect the chemical stability of the medicine and can later its physical properties. And so these products are transported via temperature controlled supply chain. There are certain considerations for a controlled temperature storage which need to be maintained while transportation:

The acceptable temperature and humidity range.

Margin of error of temperature.

Backup for temperature controls.

The layout of storage unit and airflow.

Potential areas of risks and touch points.

External temperature logging and data tracking.

Above all the temperature mapping to determine the temperature distribution under extremes of external temperature should be maintained in warehouses. All the conditions must be assured by all the parties including manufacturer, shipper and wholesaler.

5. Standards and Regulations for cold supply chain:

The companies operating within the pharmaceutical cold chain must be aware of all the set rules and standards for distribution of products in the market. These regulations can differ from country to country following it makes it complex. Specifically, manufacturer of products have direct control over the correct storage and handling of the product from the start of production till dispatch. Specific compliance is required for an effective cold supply chain structure and governance strategy are based upon combination of regularity requirements defined by corresponding regulatory bodies such as FDA, EMO, WHO, Health Canada etc.Goods Distribution Practice (GDP) is a part of quality system of warehouse and distribution process assuring that products are continuously stored, transported and handled with the set standards as required. However there are various other set protocols set to be followed at various levels during transportation, packaging and distribution of temperature sensitive products.

6.Cold Supply Chain Management Pattern:

Importance of regulation is on rise: For years the Pharma counterfeiting incidents are prompting factors for government to tighten regulations on production and supply chain. Harmonizing regulations and establishing preventive measures are some issues for pharmaceutical industries. Earlier the pharmaceutical mandates products were maintained within the manufacturer storage guidelines. The European Union guidelines (EU) established in November 2013 on goods Distribution Practices for medicinal products came into effect of extending temperature requirement to transportation. About 80 percent of pharmaproduct now require temperature controlled transportation.

Increased logistics outsourcing: For a given cost and time to manage an efficient, and reliable cold chain, the manufactures are looking forward to outsourcing. Most of the pharmaceutical companies have turned to adopt custom design solutions and just in time packaging deliveries. The formulation of third party logistics aims to make necessary changes and investment in technology, infrastructure and system drive continuous improvement to gain a competitive market edge. Specialized in Automated Search and Retrieval System (SASR) and in- situ

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X-ray verification of sensitive products are evolving demand of cold supply chain.

Training of professionals: Learning how to maintain temperature throughout the entire cold chain and meet the GDP compliance has been a complex task for the professionals. An Intricate knowledge on all aspects of cold supply chain, validation and technical expertise are a must for handling the sensitive products.

Active and Passive Shippers: Passive thermal system are typically using phase change material such as dry ice, insulated with polystyrene, polyurethane or vacuum insulated panels. With this type of configuration gel packs or similar material are used to maintain the desired temperature. On the other hand the active thermal systems are powered by electricity or batteries and are considered to be more secure during transportation. These system use mechanical energy source to control and maintain proper temperature. As a result the design helps to reduce the risk by maintain regulatory compliance. The active shippers are adding cost and higher temperature accuracy than passive shippers are most basic and cost effective.

CONCLUSION

For keeping up a cold supply chain there are successful ways which provide computerized correspondence and information accumulation. This creates a platform which links all data stored in devices to an application and gathers real-time temperature of the products currently in transit and suggests corrective what's more, preventive activities, and connects the authentic exhibition of a particular bit of bundling hardware to any stamped shipment, all simultaneously holding fast to the major worldwide administrative authorities. Manufacturers must make it sure that the drug dispenses to the customers with right quality. In India, since manufacturers don't support power over the multi layered circulation framework, the supply chain manufacturing procedure keeps on being troublesome and costly. The manufacturers are progressively understanding the significance of a viable conveyance framework in the entire process. Thus ensuring an efficient cold supply chain is a crucial step for commercialization and distribution throughout supply chain the attention should be put on training, SOP's on cold chain processes, documentation, quality assurance and its maintenance, storage conditions, temperature profiles and quality packaging methods which needs to be periodically controlled and maintained.

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