

Validation of Cold Chain Products – An essential need for Global Pharmaceutical Supply Chain

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ABSTRACT: Cold chain products are the products which requires special temperature controlled storage. Cold chain storage system is used to store vaccines, certain injectable preparations. Maintaining the temperature is necessary not only during the manufacturing but the product has to be stored up to the destination (patient). Cold chains are common in the pharmaceutical and food industries. One common temperature range for a cold chain in pharmaceutical industries is 2 to 8 °C but the specific temperature (and time at temperature) tolerances depend on the actual product being shipped. Cold chains are essential for storage and distribution of goods and temperature sensitive pharmaceuticals & biological preparations & forms an integral part of their supply chain. There is global regulatory requirement for handling, storing and distributing environmentally sensitive products i.e. cold chain products. Traditionally all historical stability data developed for vaccines were based on the temperature range of 2-8 °C. With recent development of biological products by former vaccine developers, biologics has fallen into the same category of storage at 2-8 °C due to the nature of the products and the lack of testing these products at wider storage conditions. The standardised use of qualification, validation and good cold chain management practice will be beneficial for all involved parties in handling; storing and distributing environmentally sensitive pharmaceuticals. This article reviews the increased importance of validation of pharmaceutical cold chain products and its regulatory requirement.

Key Words: validation, cold chain, qualification

The expiration date and assurance of potency of vaccines depends on the continuous control of their temperature during production and distribution. A cold chain can be managed by a quality management system: it can be analyzed, measured, controlled, documented and validated. The overall approach to validation of a distribution process is by building more and more qualifications on top of each other to get to a validated state. Validation involved both tests in an environmental chamber and actual shipping of packages by commercial overnight delivery service. This is done by executing a component qualification on the packaging components. Next an operational qualification that demonstrates the process performs at the operational extremes. The final piece is the performance qualification that demonstrates that what happens in the real world is within the limits of what was demonstrated in operational qualification limits.

The PDA's Technical Report states that a Component Qualification is required to demonstrate that a component can be manufactured to the design criteria of that individual component. This was put into the document because the industry did not understand the principles of Validation; all Validation processes were specific to equipment and not auxiliary processes such as shipping/distribution.

Performing thermal testing can also help with validating the cold chain. Certified test labs use environmental chambers to simulate ambient profiles that a package may encounter in the distribution cycle. Thermocouple probes measure temperatures within the product load to assure that temperatures do not reach outside of the required temperature range. Testing can be completed in triplicate based on a qualification protocol to create a final qualification report that can be used to defend the configuration when audited by the FDA. It is normally best to have an individual that understands the principles of Validation, when defending such processes to a Federal Regulatory body of any nation.

Cold chains need to be evaluated and controlled

- Carriers and logistics providers can assist shippers.
- The use of refrigerator trucks, refrigerator cars, refrigerator ships, refrigerator containers and refrigerator warehouses is common.
- Shipment in insulated shipping containers or other specialized packaging
- Temperature data loggers to monitor the temperature history of the truck, warehouse ect and the temperature history of the product being shipped.
- Documentation is critical.

During the distribution process one should monitor that process until one builds a sufficient data set that clearly demonstrates the process is in compliance and in a state of control. Each time the process does not conform to the process, a Non Conformance or Deviation should document each event. Those events should be properly investigated and mitigated so that they do not occur on future shipments. Thus the process is continually evolving and correcting for anomalies that occur in the process. Eventually the process can evolve into periodic monitoring once sufficient data demonstrates that the process is in a state of control. Any anomaly that occurs once a process is in a state of control will result in the process being invalidated and not in control and result in product withdraw from the market to ensure patient safety.

It is necessary to develop an internal documentation system as well as multi party communication standards and protocols to transfer or create a central repository or hub to track information across the supply chain. These systems would monitor equipment status, product temperature history, and custody chain, etc. These help

ensure that a food, pharmaceutical, or vaccine is safe and effective when reaching its intended consumer.

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