RCA Designs a Shipping Validation Study for a Pharmaceutical Company with Two API Manufacturers Located in Europe

Client:

Midsize start up

Industry:

Pharmaceutical

Business Challenge:

Design a study that proves the SQuIPP of the drug product is maintained throughout the multi-national manufacturing and distribution process given the multiple modes of transportation

Project Timeline:

20 months

About Shipping Validation Studies

Many medicinal products, intermediates, APIs, and diagnostic products require storage at specified temperatures in order to maintain product SQuIPP (safety, quality, identity, purity, potency). They are also regularly being shipped all over the world, therefore requiring temperature-controlled transportation, also referred to as “cold chain distribution”. In 2005, PDA released Technical Report No. 39 on Cold Chain Guidance to provide the industry with the essential knowledge and practices needed to design and qualify a reliable cold chain shipping process. When designing the process, it is important to keep in mind the principles of qualification for transport of temperature-sensitive items:

- Development of specifications, processes, systems, and components
- Written procedures
- Approved protocols and reports
- Justified test methods and acceptance criteria
- Qualification testing that challenges “anticipated extremes”
- Ongoing monitoring or periodic evaluation
- Change control

Shipping validation studies are used to conduct qualification testing. The studies reflect actual transportation load conditions and configurations, and are executed seasonally (summer and winter) to capture “anticipated extremes”. There must be ample data, consistently generated over multiple shipments, to support that the shipping process is capable of maintaining product temperature within the required temperature range throughout transport and does not impact the product SQuIPP. This data is captured by strategically placed temperature monitoring devices which monitor and record the drug product temperature and free air space temperature throughout shipment. After receipt and

review of the temperature data following the shipments, it can be determined whether the cold chain shipping process designed is qualified for thermally-controlled transport.

Client Challenge

A pharmaceutical start-up, located in the USA, has a novel drug. They approach RCA to design their shipping validation study given the complexity of their supply chain, manufacturing, and distribution process.

The challenge is to design a study that proves the SQuIPP of the drug product is maintained throughout the multi-national manufacturing and distribution process given the multiple modes of transportation and multiple handoffs between four different companies. The company has two API manufacturers, located in different parts of Europe, that they wish to qualify using both air and sea transportation between Europe and Canada. The finished drug product is to be manufactured in Canada by a different company and then shipped to the USA by either air or ground transportation for distribution by yet another company.

RCA Approach

Based on the request of the client, this was not just one shipping study, but multiple. Each API manufacturer needs to be qualified for each route using different modes of transportation, and each route needs to be challenged by "anticipated extremes", which in this case is summer and winter temperatures. There were a multitude of shipping configurations (# of drums, drum sizes, drum weights, # of pallets per container, types of containers, etc.) that differed by manufacturer, but in some cases also changed within the same manufacturer, that added complexity to this project. Additionally, any possible new challenges associated with international shipping practices had to be identified (languages, time zones, holidays, etc.). The critical parameters involved for each shipment were previously outlined by the client. These parameters include:

- Transportation (duration, modes, routes)
- Product Stability (temperature range established)
- Packaging (bulk or finished goods)

Based on this information, RCA was able to generate multiple shipping study protocols to fit the company's needs. These protocols included representative transportation load configurations, defined packaging configurations, and calibrated temperature monitor positioning. Given the delicate nature of the API, lot samples were pulled and sent with each shipment to undergo chemical testing following shipment. The testing results were used as further evidence to illustrate that the SQuIPP of the API material was not impacted by the shipment. Because the client would not be at each CSP site to facilitate the validation shipments, it was imperative that the protocol provided clear instructions and diagrams (in the appropriate languages) to ensure temperature monitor placements and pallet configurations were accurate.

Given the complexity of the data collection, the pharma company also asked RCA to collect and analyze the shipping data. Multiple different companies were involved in manufacturing and distributing the finished product, therefore, the handoffs had to be effectively managed. Each company involved was required to provide documentation to RCA illustrating their responsibilities outlined in the protocol had been followed. Given that the product is temperature-sensitive, a delayed or missed handoff puts the product at risk. It was RCA's job to analyze the shipment documentation and temperature data to determine whether the validation passes and generate the final reports.

Results

The pharma company was able to provide sufficient data proving the drug product and drug product material was maintained within the established temperature range throughout the cold chain distribution by all modes of transport (land, sea, and air) during both winter and summer seasons. The data also illustrated the SQuIPP of the product was not impacted during the shipments. The thorough design of the study, combined with data tracking and analysis from RCA, enabled the company to prove this consistency over time.

With this milestone achieved, the company became attractive buyers, and has since become a wholly owned acquisition of a large pharmaceutical company.