

Maintaining Integrity of the Pharma Cold Chain

Two years since the start of the Covid-19 pandemic, the social and economic implications are still being felt on a global scale. The pandemic has impacted practically every phase of our lives and it also greatly influenced the cold chain logistics industry bringing new challenges and requirements.

It's been a challenging time, but also a time with significant achievement within the pharma and transport industries. The Covid-19 vaccine development was much faster than any other vaccine in history, with production and distribution at unprecedented scale. Vaccine manufacture reached close to 1.5 billion doses per month according to the WHO,¹ creating pressure for ultra-low cold chain considering the fragility of mRNA vaccines – where ultra-cold storage helps to slow down the chemical reactions that can tear them apart.

This challenge is predicted only to get bigger as mRNA vaccine technology is applied to tackling other diseases – from cancer and flu to malaria and HIV. It's a technology that's revolutionising the pharmaceutical sector and ushering in a new era of vaccinology. This gives a clear sign that ultra-cold temporary storage, as well as 15–25°C and 2–8°C temperature ranges will be a common need for pharmaceutical transport and logistics into the future.

Delivering confidence in the reliability of refrigerated pharmaceutical transport is key. Pharmaceutical companies rely more on partners that can offer the end-to-end solutions to ensure their products arrive safely at their destination – traveling across all modes of cold chain transport. These partners help fully understand the range of potential temperature requirements and their implication for logistics – mapping map out the supply chain, identifying potential bottlenecks and planning end-to-end innovative solutions.

This also highlights the importance of Good Distributions Practice (GDP)

Regulations as a key factor in maintaining safety, integrity and efficacy of all biopharmaceutical products – not only the Covid-19 vaccines.

GDP Regulations – Protecting Biopharmaceutical Shipments

By some estimates, as many as 70 percent of products require some type of controlled temperature environment, including those that need to be maintained at a consistent “room temperature.” For most medical and biological products, the GDP guidelines require a temperature-controlled environment for several stages of manufacturing, shipping and storage.

For a Cold Chain Solution Provider, Focusing the 4-stage GDP Qualification is a High Priority.

Regardless of the mode of transport, it should be possible to demonstrate that the medicines have not been exposed to conditions that may compromise their quality and integrity. This requires a risk-based approach when planning transportation. If a deviation such as temperature excursion or product damage has occurred during transportation, it should be reported to the distributor and recipient of the affected medicinal products. A procedure should also be in place for investigating and handling temperature excursions.

Temperature-sensitive products should be transported in qualified equipment (e.g.

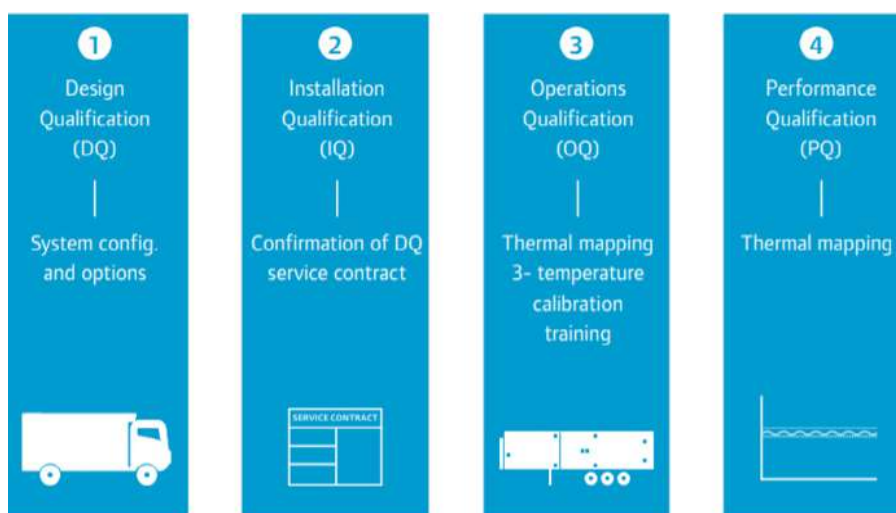
thermal packaging, temperature-controlled containers or temperature-controlled vehicles) to ensure correct transport conditions are maintained between every step of the way – from the manufacturer, through the wholesale distributor and when reaching the customer.

When using temperature-controlled vehicles, the temperature monitoring equipment used during transport needs to be maintained and calibrated regularly. Leading operators are equipping their fleets with integrated asset management systems that protect shipments by establishing critical controls at all points in the supply chain. Temperature mapping under representative conditions should also be carried out and should consider seasonal variations.

The leading transportation refrigeration providers, enable customers to access information that demonstrate products have complied with the temperature storage conditions. The key elements of the site qualification and validation programme should be clearly defined and documented in a validation master plan (VMP) or equivalent document. And of course, qualification and validation activities should only be performed by suitably trained personnel who follow approved procedures.

There are four stages of qualification outlined in the guidelines and they include:

- **Design Qualification (DQ)** – where the compliance of the design with good





END-TO-END PHARMA TRANSPORT SOLUTIONS



manufacturing/distribution practice (GMP/GDP) should be demonstrated and documented. The equipment used is suitable and meets relevant criteria.

- **Installation Qualification (IQ)** – confirms that the equipment is installed and conforms to the approved design qualification and include but are not limited to:

- Verification of the correct installation of components, instrumentation, equipment, pipe work and services against the engineering drawings and specifications
- Verification of the correct installation against pre-defined criteria
- Collection and collation of supplier operating and working instructions and maintenance requirements
- Calibration of instrumentation
- Verification of the materials of construction.

- **Operational Qualification** confirms that the equipment performs as designed throughout the anticipated operating ranges and provides operating guidance. This includes:

- 3-temperature points calibration check of each equipment
- Operating guidance on the equipment usage
- Training for fleet operators, drivers and distribution managers around efficient loading practices, operating

procedures, preventative maintenance strategies.

- **Performance Qualification** provides mapping test results that prove that the equipment can perform effectively and reproducibly, based on the approved process method and product specification. This includes:

- Test conditions
 - Worst case scenario
 - Empty load space
 - Extreme Ambient temperatures: -30°C to +45°C
 - Test in climatic chamber
 - Better control of test conditions
 - Winter and summer tests to be done at the same time
 - Number of sensors:
 - 20 to 25 sensors in a vehicle (ATP standards)
- Qualification at 3 temperature ranges
 - +15°C to +25°C / +2°C to +8°C / under -20°C, under -70°C.
- For Last Miles distribution
 - Additional tests with multiple door openings, empty and loaded tests, failure mode
- An extensive range of tests in climatic chamber to ensure the simulation of worst-case scenarios in real life conditions.

These guidelines should be consulted in order to ensure appropriate procedures are

followed and measures taken to maintain product quality throughout the cold chain and limit risks during transport.

Each temperature-controlled transport unit used for the transportation of pharmaceutical products needs to go through a qualification process.

Qualification consists of a temperature validation process that maps the temperature performance of the unit operating in particular temperature ranges. Temperature sensors are placed in a number of locations throughout the box to identify if there are any hot or cold spots that could affect the transportation of the pharmaceutical products and to show that the equipment is suitable to operate in worst case scenario within upper and lower limits.

Once the tests are completed, it is essential to complete the process of qualification by preparing the adequate documentation that ensures that the four stages of qualification have been completed correctly. At this time, a certificate can be provided to prove that the equipment is qualified for pharmaceutical operation.

Considerations Before or During Transport of Pharmaceutical Products

Preserving cold chain integrity and maintaining product quality will remain an increasing challenge for pharmaceutical companies and their partners in handling and transporting pharmaceutical products globally. As temperature-controlled shipments grow in volume and regulatory requirements change, pharmaceutical and biotech manufacturers need the support of their transportation industry partners



to ensure compliance with regulatory requirements and the safety and integrity of their high-value shipments. Each cold chain partner company should always have a GDP-Trained Responsible in their team. This person should be regularly trained using a combination of general GDP awareness and technical/operational training on the different cooling units and basics of temperature-controlled transport.

Other important factors to consider before or during transport of pharmaceutical products are:

- Load space configuration when the trailer body design is carried out, such as whether to include dividing doors,
- Drivers are required to be trained to air shoots, return air bulkhead design.
- The load space should be kept clean at all times and only cleaning agents that will not affect the cargo should be used.
- To conform to temperature monitoring and recording obligations, the units are required to have on-board temperature recording and monitoring as well as printed delivery point tickets to prove the temperature integrity of the load space.
- Because the products have to stay within a particular range, both temperature and air management must be controlled within this range with no deviation allowed or any excursions limited to manufacturer specifications.
- Drivers are required to be trained to show that they can operate the unit within the GDP requirements.
- Regular maintenance and service records should be kept for inspection if required by the pharmaceutical companies.
- A calibration check should be completed at least once per year; individual pharmaceutical companies may request more checks. A three-point calibration of the sensors is important to ensure that when the unit is operating it can maintain the load space temperature at the set points as listed above.
- To prevent risk of contamination to sensitive shipments in the compartment, cleaning standards in line with GDP guidelines should be enforced under the guidance of certified service personnel.



For cargo as precious and sensitive as life-saving medicines, active controls that can monitor for temperature, humidity and location are critical. With the solutions and technology that exists today, customers can be confident of the efficacy of their product while in transit or in storage.



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