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Cold Chain Logistics: Passive vs. Active Systems in a globally disrupted age

A non-biased review of the developing market by 10 industry leaders

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Straight talking

With the ever-growing demand for cold chain distribution, compounded by the COVID-19 pandemic, we explore the Active, Passive and Hybrid Temperature Controlled Packaging options. This white paper will provide practical advice on where and when temperature-controlled packaging should be used in a global pharmaceutical supply chain. We will give detailed insight into the topic from leading industry experts from all supply chain stakeholders.

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Introduction

Technology with regard to medicines is advancing at an astonishing rate, particularly with the growth of the biotech industry. This is illustrated with the fact that the pharmaceutical logistics industry is expected to grow at a rate of 8.5% through to 2028. Cold chain logistics accounts for over a quarter of the total spend on pharmaceutical logistics, which is fuelled by the growth in demand for temperature-controlled products.[1]

Choosing the right packaging option to maintain the vrequired temperature of the shipment is a vital part of pharmaceutical supply chain compliance.

[1] https://www.grandviewresearch.com/industry-analysis/pharmaceutical-logistics-market

8.5%

The expected compound annual growth rate (CAGR) of the global pharmaceutical logistics market from 2021 to 2028

Grand Review Research

$35B

The amount the biopharma industry loses annually as a result of failures in temperature-controlled logistics

Institute for Human Data Science

52%

of all temperature excursions occur whilst a shipment is under the control of an airline or within the airport environment.

IATA

Overview of Packaging Options

Active Packaging Systems

Active packaging is a system that uses mechanical or electric systems powered by an energy source, combined with thermostatic control in order to maintain proper product temperatures.

What is an active unit?
Active packaging systems are shipping containers with a hard, insulated exterior shell. Active packaging systems come in different forms, typically in Unit Load Device configurations.

What does it do?
The active packaging system allows for set temperatures to be configured on the unit. By means of a thermostat, it maintains the temperature within specified limits around the enclosed product. To put it simply, an active packaging system is a mobile refrigerator. Active packaging systems can be further defined as 'cooling only' and 'heating/cooling systems'.

How does it work?
Let's look at 'cooling only' containers first. A 'cooling only' container system typically uses either dry ice or phase change materials (frozen gel pack refrigerants) as the cooling mechanism to maintain refrigerated and frozen conditions around the product. Internal temperatures are held within the tolerance through the use of mechanically operated circulating fans. These fans are battery powered and therefore a power source is required to charge the battery.

The 'heating and cooling' containers use compressor or dry ice for refrigeration along with electric heating coils to maintain tight air temperature tolerances around the product. Again, these systems can be set at a predefined temperature and through the use of temperature monitoring devices, the unit can control the internal temperature based on fluctuations of the ambient temperature. The units are also battery powered so an electrical source is critical to ensure the battery can be charged.

Examples: Envirotainer, C-Safe, and Dokasch.

"For some reason if it's expensive, passive does work but they go with active."

Roger Chew
Global Sales Director,
SFS PHarma Logistics

Passive Packaging Systems

What is a passive packaging system?
Passive packaging systems consist of materials intended to keep the internal contents of the package within a specific temperature range for a defined period of transport without any means of mechanical assist. Passive packaging systems generally comprise two main components, which are insulation and coolants. The internal temperatures are maintained by means of temperature stabilizers or other phase change materials (PCMs).

What does it do?
The packaging system protects the contents from the surrounding environment, maintaining its temperature within an acceptable range for a defined period of time, despite variable external temperature extremes. The insulation separates the contents from the environment and the thermal energy storage system maintains the temperature within the package by releasing or absorbing thermal energy.

How does it work?
PCMs are used to store and release thermal energy during the process of melting and freezing (changing from one phase to another). When such a material freezes, it releases large amounts of energy in the form of latent heat of fusion, or energy of crystallistion. Conversely, when the material is melted, an equal amount of energy is absorbed from the immediate environment as it changes from solid to liquid. By using materials with appropriately designed melting and freezing points, the internal temperature of the packaging system can be kept within a defined range for a period of time.

The packaging insulation system slows down any effect of external temperature extremes and, in conjunction with the PCMs, extends the time that it will hold the contents within the specified temperature range.

Passive packaging systems have a predefined validated time period, typically based on shipment transit time and therefore must be transported quickly through the supply chain. As with an Active packaging system, there are different types of Passive packaging systems. There are single use packaging systems and reusable systems. We will look at each in turn.

Single Use Passive Packaging Systems

Single-use, or disposable systems, are designed to be used once in order to transport goods within a specified temperature range for the duration of a single destination trip. The packaging system then needs to be disposed of on completion of the journey.

These systems typically involve a flexible outer packaging, such as cardboard, an internal insulating barrier between the outer packaging and the product, usually expanded polystyrene, and a thermal energy system, such as gel or ice packs.

These systems tend to be utilised for smaller product volumes and distributed supply chains where return of the packaging system may be difficult to manage. However, this does create a waste stream that needs to be managed.

"When active goes **it's a catastrophe.**"

Mike Meakin
Vice President, Global Quality
Regulatory & Compliance, DHL Supply Chain

Reusable Passive Packaging Systems

Reusable systems are more robust and are designed to be used on multiple journeys. They range from 'semi reusable' systems, which may be used on a few occasions before damage or wear and tear would require components of the system to be replaced, to rigid robust systems designed for constant reuse and years of trouble-free service.

The outer part of the packaging system can be constructed from lightweight materials, such as Correx® boxes, or moulded medium/high density polyethylene shells that give significant impact resistance and product protection. Insulation systems vary from the use of pre-formed components, such as vacuum insulation panels (VIPs) lining the package, to integrated polyurethane foam encased in the outer packaging layer.

Depending upon the desired temperature range, different thermal energy storage systems are routinely employed. PCMs are normally used in a rigid moulded polymer plate and can be conditioned to a particular temperature on multiple occasions, making them flexible and easy to use for temperature ranges typically from -25°C through to +25°C. Dry ice (the solid form of CO2) is customarily used for temperatures ranging from -80°C to -60°C and is normally enclosed in a reusable or cardboard container within the outer packaging layer.

Data loggers are often integrated into these packaging systems, monitoring the internal contents and external temperatures, and recording the transported product's temperature at all stages of its journey to ensure compliance and traceability. It is important to note that for any Passive packaging solution, the system's performance i.e., its durability and longevity, is based on the type of insulation used, the stabilizers/refrigerants, the ambient temperature exposure of the shipment whilst in transit, the mass of the load packed into the passive packaging system, and finally the staging temperature of the materials that form the complete pack-out at the time of loading.

Example: Tower Cold Chain

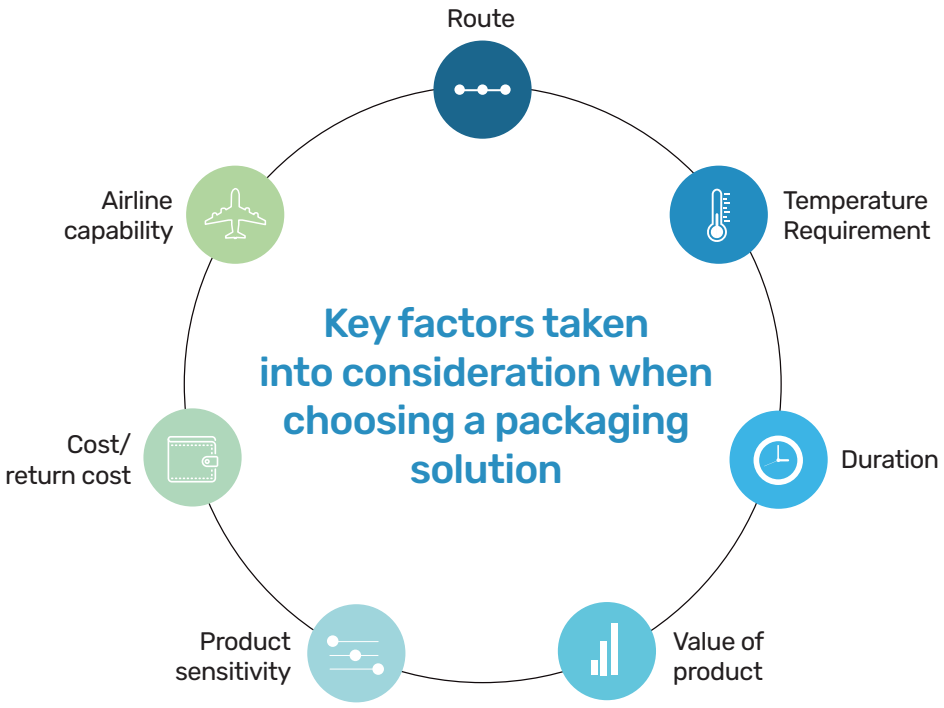
Hybrid Packaging Systems

What is a hybrid packaging system?
Hybrid packaging systems are simply a combination of the technologies of both active and passive containers. Visually the packaging systems appear similar to active containers but utilize phase change refrigerant materials.

What does it do?
By utilising both active and passive technology, the unit prolongs the validation period through the use of phase change materials in combination with the mechanically powered cooling/heating systems.

How does it work?
As with an Active unit, the system can be set at a predefined temperature, and through the use of temperature monitoring devices the unit can control the internal temperature. These systems typically use the coolants to bring down the temperature when necessary and electrical heating units to raise it, which is regulated by a thermostatic control to maintain proper product temperatures.

Example:
SkyCell



Modal Choice

According to the EU GDP guidelines, products must be shipped under the label claims. In other words, the temperature detailed on the outside of the product packaging must be maintained throughout a shipment's journey.

Building a robust temperature sensitive supply chain is critical to maintain product quality, efficacy and safety. In the freight forwarding and logistics industry, the choice of transportation mode must be determined using a risk-based approach. As pharmaceutical manufacturers are relying extensively on their service providers to provide this expertise, the choice of mode and temperature-controlled packaging combination become critical.

Designing, developing and implementing a temperature sensitive supply chain is paramount to a successful shipment. Freight forwarders and logistics providers should be ensuring that the routes and lanes that they have responsibility for are mapped and assessed for risk from end to end. According Kamil Rarak, Special Cargo Product Development and Training Manager/Head of PharmaOPS Team, LOT Polish Airlines, "it's about assessing risk using the Critical Control Points across the Supply Chain."

The choice of temperature-controlled packaging solution is based upon many critical factors, such as transport mode, route, external temperature cycle and duration.

Road and air transportation have long been the chosen methods of transportation when shipping pharmaceutical products. Both modes provide robust solutions of flexibility and speed and, as such, the choice of temperature-controlled packaging solution is critical for each mode. For example, with air transportation, the risks include tarmac transfer, airside loading and unloading.

According to IATA, 52% of all temperature excursions occur whilst a shipment is under the control of an airline or within the airport environment. In fact, according to the Institute for Human Data Science, the biopharma industry loses approximately $35 billion annually as a result of failures in temperature-controlled logistics. The challenge of the airport apron and its susceptibility to excessive temperatures is compounded by the high cost of thermal dollies traditionally used to ferry pharmaceuticals across the tarmac. route, external temperature cycle and duration.

However, new players in the pharmaceutical logistics industry have started to depart from these expensive and bulky solutions. In early 2020, Rome-based company, La Couverture, introduced their hybrid product and namesake onto the market. Although thermal covers are no strangers to the tarmac apron, La Couverture's comprehensive design incorporates four layers of sustainably sourced insulation that seeks to upscale this more affordable system of airport temperature control. Innovations on the airport apron, however, are still in their infancy due to the sheer scale of existing global airport infrastructure, and as a result transit "should be avoided when achievable," Michał Grochowski told a recent round table discussion sponsored by Tower.

When we look at road freight, the risks here are the heavy reliance on the driver with regard to the temperature-controlled technology used by the vehicle, the risk of equipment failure and loading/unloading/cross-docking of temperature sensitive pharmaceutical shipments.

However, times are changing and as Health Authorities have increased the pressure on reducing prices, manufacturers have been forced to reduce their own costs and have turned to the relatively affordable option that ocean freight offers. Along with costs, ocean freight also provides a very stable option when it comes to transporting pharmaceutical products. Certainly, from a temperature perspective, assuming the correct temperature-controlled packaging solution is used, in conjunction with a reefer container, product and shipment temperature can be maintained at a constant level throughout the journey.

Whatever mode of transport is chosen, it is important to note a risk-based approach should be taken when planning transportation. We will discuss the topic of risk later in this Whitepaper but for the purposes of planning transportation, the logistics service provider must understand the customers' requirements to include but not be limited to, product type, product temperature requirements, the origin and destination, size of the shipment and value of the shipment. Not until these requirements have been documented and understood can a suitable mode of transport and temperature-controlled packaging solution be implemented.

"It's about assessing risk using the Critical Control Points across the Supply Chain."

Kamil Rarak
Special Cargo Product Development and Training Manager/Head of PharmaOPS Team, IATA CEIV Pharma

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"The main variables that will be factored in during decision making are the sensitivity of the product itself (including stability data), the climates at origin and destination, and the size and value of a shipment."

Darren Sherlock
Regional Operations Manager (ROW)
Virgin Atlantic Cargo

Collaborative Approach

Because of the increasingly complicated requirements put in place to ensure product integrity is maintained throughout the entire supply chain, we have seen a shift towards collaborative partnerships between all key stakeholders within the logistics industry. This has led to the development of strategic hubs and 'pharma corridors', in which groups of GDP compliant companies work together to offer customers assurance that their product will be handled with compliance and consistency from start to finish.

However, the pandemic and vaccine rollout has called to attention this defined 'start to finish' process. Multiple exposés of the vast quantities of unused vaccines in western countries point towards a need to re-evaluate the logistical ease and efficiency with which vaccines can be redirected to less vaccinated populations. Mike Meakin, Vice President of Global Quality Regulatory & Compliance at DHL Supply Chain, highlights the need for the industry to collaborate in order to react to this necessary 'surplus transportation', both in the current COVID-19 vaccine climate and beyond.

The building blocks for a more collaborative and therefore reactive global supply chain have, however, started to be built. Partnerships made between the likes of Emirates Skycargo and Maestro, Brussels Airport Company and Hong Kong International Airport in 2019, have proved to be prescient initiatives in light of the outbreak of the pandemic. More recently, collaborative efforts between the freight giant Dubai Airports and GMR Hyderabad in South Asia's pharma capital, are continuing a momentum to bolster 'pharma corridors' between CEIV Pharma certified airlines and respective handling communities.

The challenge for the pharmaceutical logistics industry here is to further broaden these corridors globally into, say, parts of Africa where the ascendency of perishables in national imports and exports means that cold chain infrastructures have a more limited portfolio. Roger Chew of SFS Pharma Logistics, and a leading figure in the Asian pharmaceutical logistics sector, expressed similar cautionary words given the still gradual transferral of cold chain 'know-how' in the East.

Regardless of geography, environmental conditions of the shipped product need to be managed to prevent any excursion during transportation. This is accomplished using active, hybrid or passive thermal packaging, which has been qualified from origin to destination - for the time and temperature of the specific shipping lane. Details of the temperature monitoring should be justified using the proper loggers and/or qualification data. Realtime data loggers should be considered – which could allow for real time corrections over the entire shipment process.

Managing Risk and Cost in a Global Supply Chain

As pharmaceutical supply chains become far more complex and truly global in nature, the management of risk becomes far more critical. Assessing, Controlling and Reviewing risk are key elements of the process of Quality Risk Management. Therefore, conducting an effective Route Risk Assessment becomes an important exercise in the shipment of time and temperature sensitive pharmaceutical products. "Conducting route risk assessments will determine the best type of packaging to use," according to Kamil Rarak from LOT Polish Airlines. This key exercise and activity is further emphasised by Don Riach, Director UK Operations, Biocair, a specialist Good Distribution Practice Courier, who states that "Route Risk Assessments are a fundamental to the choice of packaging system."

Risk can occur at multiple points across a pharmaceutical supply chain, and it must be managed effectively. The use of the correct temperature-controlled packaging solution mitigates the risk of temperature fluctuations and extremes.

According to Jeff Beck, Global Head Supply Chain, Head of the Americas, and Lisa Barbieri Moher, Head of North America Distribution Package Engineering and Graphics, at Sanofi, "Regardless of container, there is always risk in play. We are comfortable in using all types within our portfolio that have been qualified. The risk of mishandling due to human error, or delays on tarmac, customs, handling upon receipt are always there. We do our best working with freight forwarders and our customers to mitigate as much of that as possible."

The choice of temperature-controlled packaging also has risks. This is highlighted by Brendan Beech, Director Global Networks and Business Development, Maltacourt Global Logistics, who states when using an Active Packaging system that "if something goes wrong it's game over". Brendan further mentions in "the use of passive packaging systems, in my experience, not many things go wrong."

Therefore, the choice of packaging system and who makes that choice is also vital to a secure and compliant supply chain. In most cases, the choice of packaging system is determined by the Pharmaceutical Manufacturer themselves, but as we have highlighted earlier, the choice is very much assisted by the experiences of the individual supply chain stakeholders, freight forwarders, airlines, shipping lines, trucking companies, etc.

"We are very much guided by customer requirements," according to Brendan Beech, Maltacourt. This opinion is also echoed by Kamil Rarak, LOT Polish Airlines who states, "the decision on the type of solution is determined by the shipper and the type of service offered by the airline." Darren Sherlock, Regional Operations Manager (ROW) from Virgin Atlantic Cargo,

> **"Passive is cheaper and more flexible** when building consolidations"
>
> **Brendan Beech**
> Director – Global Network and Business Development, Maltacourt Global Logistics

states, "Packing decisions tend to be made further up the supply chain, by shippers and/or freight forwarders based on risks identified on a particular journey or route. The main variables that will be factored in during decision making are the sensitivity of the product itself (including stability data), the climates at origin and destination, and the size and value of a shipment."

In some cases, as with DHL Supply Chain, the choice of packaging "is dependent on the distribution model," according to Mike Meakin, but typically "manufacturers drive the decision."

It isn't just risk that influences the choice of packaging. There are several other critical elements to consider. Maik Slijpen, Director, Value Stream Management at the Janssen Pharmaceutical Companies of Johnson & Johnson, identifies "two impacts; the first is risk and the second is cost, for example, distributing vaccines for humanitarian aid, cost is critical. Therefore, we use passive packaging solutions for most of these shipments, which can be as much as 40% cheaper in comparing it to active." Cost also has an influence on both the freight forwarding and airline industry. Roger Chew from SFS Pharma explains that "active units are typically calculated on pivot weight." Don Riach from Biocair also explains the impact of the use of an Active Container and the effect that "an active container is billed on pivot weight."

Cost also has an impact within the Air Cargo sector. Darren Sherlock highlights that one of the downsides of an Active Container is "the costs – leasing costs for these units are high, and the weight of the units means shippers will pay not just for the shipment weight, but also for the tare weight of the container too... Reverse logistics of the empty container is the hot potato that neither shippers, forwarders or airlines want – so costs for this must also be factored in to active container rates, especially when revenue cargo is displaced on the return flight." LOT Polish Airlines' Kamil Rarak also highlights the impact of cost. He states that, "cost is very much a factor in regard to the choice of packaging solution, as is the size of shipment."

Remote Locations

The COVID pandemic highlighted the importance of the pharmaceutical supply chain. Perhaps up until this point, how medicines for human use were delivered to patients was relatively unknown. Certainly, within the logistics industry, not only was working remotely a significant challenge but also the lack of freight capacity compounded a very difficult situation. This was discussed at the recent Tower Cold Chain roundtable discussion and described extensively by Michal Grochowski of LOT Polish Airlines.

The pandemic has highlighted the challenge to get medicines delivered to both developed and developing countries in a secure and efficient way. Despite the challenge, many opportunities have arisen and none more so that in the Temperature Controlled Packaging sector.

As we have already discussed, there are several factors that influence the choice of packaging solution: risk, cost, mode etc., but perhaps one of the most important influences is location and route.

According to Maik Slijpen from Janssen Pharmaceuticals, "Destination is a critical decision factor in regard to packaging. Packaging solutions can be different dependent on the destination country." Don Riach, from Biocair, echoes the opinion of Janssen Pharmaceuticals and emphasises that "it is not only the destination of the shipment but also the airline's capabilities to that destination that influence the choice."

With the demand for medicines increasing globally, particularly from developing countries, the reliability and availability of temperature-controlled packaging solutions is a very important consideration. There can be significant global variations in the type and availability of airport infrastructure, as highlighted by Mike Meakin, DHL Supply Chain, at the recent Tower roundtable discussion. The topic of airport infrastructure will be discussed in a future white paper.

Temperature Controlled Packaging, as we have seen, is used to reduce the risk of temperature deviations and excursions in the supply chain. We typically use packaging to provide control to an uncontrolled process. The challenges faced by pharmaceutical supply chain in delivering products in a controlled way can be further compounded when delivering product to remote locations. According to Jeff Beck and Lisa Barbieri at Sanofi, they believe that a passive packaging solution may well be the only option. "Some developing countries are already there, as they cannot accommodate active solutions, or, due to plane size, they cannot accommodate active solutions. For sure, especially when we consider how fast technology is moving forward (i.e. drone delivery)." Maik Slijpen from Janssen Pharmaceuticals shares the same opinion. "Definitely passive. Passive containers do the job, it works. They are much easier to handle at distribution centres."

Interestingly, many of the other key players in the pharmaceutical supply chain have the same opinion. When deliveries need to be made to remote locations where infrastructure is not available to support a compliant supply chain, the use of a passive packaging system wins out. Certainly, within the freight forwarding and specialist courier market, the use of a passive packaging system provides greater reliability and performance.

Another important factor to consider in regard to compliance, is training. Over the past few years there has been an increased awareness of the need for greater compliance within the pharmaceutical logistics industry. One of the key initiatives has been the introduction of the IATA Center of Excellence for Independent Validators in Pharmaceutical Logistics (CEIV Pharma). The certification has the aim of creating a global standard across the Air Freight sector. This initiative, along with the use of external training experts, has had a significant effect in increasing the levels of knowledge, experience and compliance at a global level.

An important element to consider, as part of any training programme, is the appropriate training in regard to the use of Temperature Controlled Packaging systems. Many of the established Active, Hybrid and Passive Packaging providers offer in depth training on their different products and how they should be used to ensure product quality.

"The use of passive shippers gives **greater access to developing countries**"

Maik Slijpen
Director, Value Stream Management,
The Janssen Pharmaceutical Companies
of Johnson & Johnson

Key pillars of concern in a changing market

Conclusion

It is very much the responsibility of all stakeholders in the pharmaceutical supply chain to ensure patient safety. In this white paper we have explored the topic of temperature-controlled packaging solutions. We have identified the different types of solutions available today, whether that is Active, Hybrid or Passive. Each solution has its own place in the logistics chain.

Through the valuable input and experience of a number of the industry's leading experts, from all areas within the supply chain, we have highlighted how Quality, Risk, Cost, Collaboration, Training and Compliance ensures pharmaceutical and healthcare products reach the patient.

In a supply chain increasingly global in nature, we must make the right decisions to ensure product quality, safety, efficacy and integrity.

About this white paper

This white paper is the first in a series providing the industry with unedited, unbiased informative industry insights from leading industry figures in their respective fields.

Find out more

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Schedule a meeting
If you would like to schedule a meeting to discuss your specific needs based on the topics raised in this white paper, please contact:

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About Tower Cold Chain
Tower delivers proven physical and temperature protection for pharmaceutical and life science products. Our robust, reliable and reusable containers are the essential link in the stability of the cold chain.

Headquartered in the UK, we operate a global network ensuring availability and easy access to our products for all customers.

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