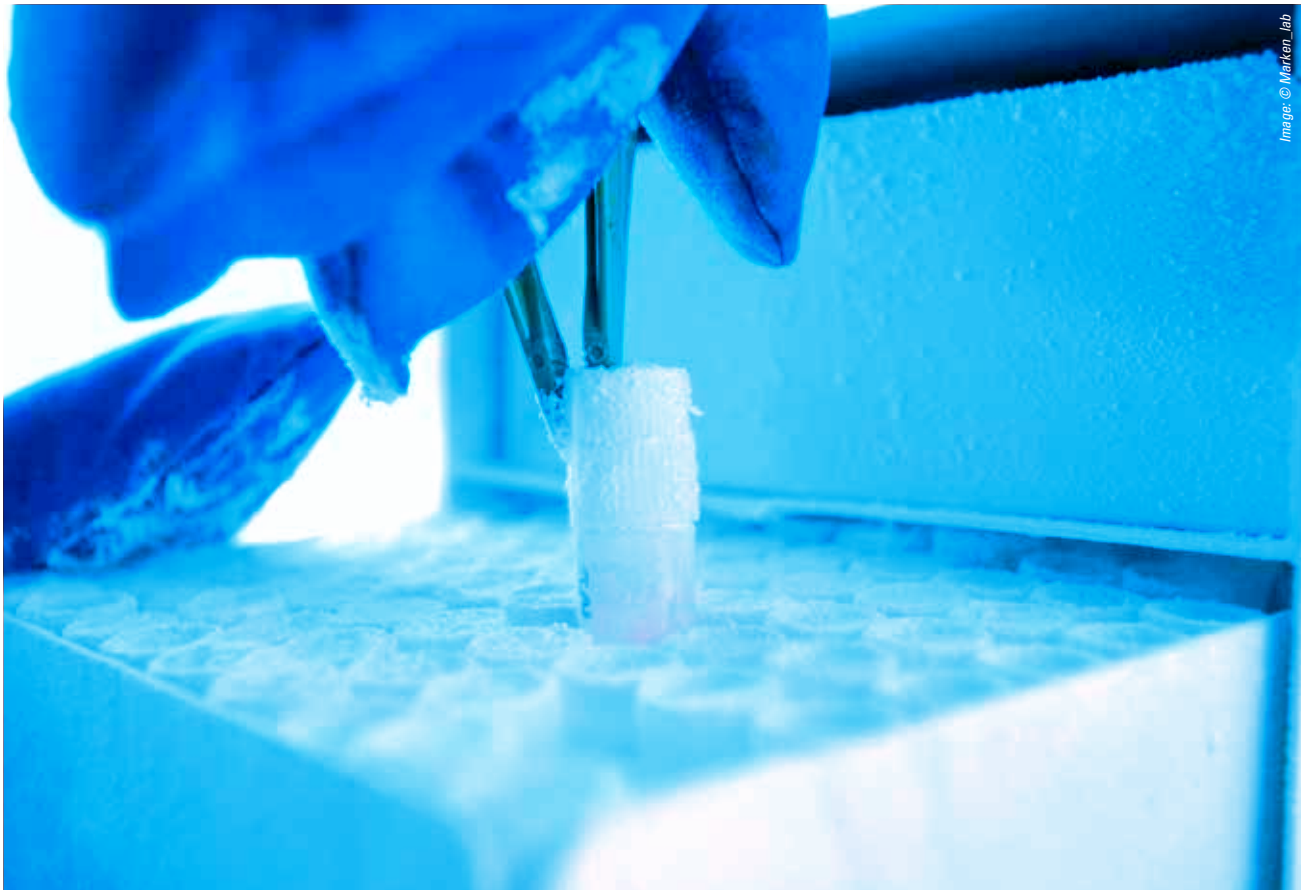

It's All in the Air

There are many ways to deliver pharmaceuticals, and each method comes with its own temperature management concerns. But how do you know which procedure to choose, and how can you make it compliant and cost-effective for your goods?

Mark Edwards at Modalis

The transport of pharmaceutical products used to be relatively straightforward. Almost all products had temperature instructions on the packaging (also known as the label claim) – such as "store below 25°C" or "do not freeze" – but this was largely ignored during transportation as general consensus held that this only applied to storage, not distribution. Vehicles, containers and the like were expected to be clean and in good condition, but that was about the extent of the quality requirements.

Cold chain – or products with a label claim between 2 and 8°C – was treated rather more seriously so shipments were usually subject to some form of temperature protection; be that either the vehicle itself or the secondary packing being used to mitigate the risk of a temperature excursion outside of the label claim.

EU GDP Guidance

Gradually, the industry began to realise that serious problems could arise from the way products were transported, and a new set of Good Distribution Practice (GDP) guidelines was needed. Updated EU GDP guidelines were released in November 2013, with other countries – such as the US, Singapore and Australia – issuing their own versions. Compliance has been an ongoing challenge for many companies ever since.

Different organisations have taken various approaches, highlighting the ambiguity and flexibility inherent in the guidelines. Some have interpreted them to mean that all products require temperature control and have implemented this across their international supply chains. Others have taken the following paragraph from Section 9.2, and used it alongside stability data to justify their current

Temperature/Service	Active container	Airline pharma service	Passive container	Blanket	No protection
2-8°C high value	√	X	X	X	X
2-8°C low value	X	√	√	X	X
15-25°C high value	X	√	√	X	X
15-25°C low value	X	X	X	√	√

Table 1

(pre-updated GDP) practices: "Risk assessment of delivery routes should be used to determine where temperature controls are required." Some are even looking to modify the label claim temperatures in their marketing authorisations to avoid instigating any logistics changes.

Regulators have come forward with differing interpretations of some sections – for example, the UK's Medicines & Healthcare products Regulatory Agency advises that transport is an extension of storage and that a wholesaler dealer licence should be present for products remaining *in situ* beyond 36 hours. Other EU authorities state different times, with a common quote being 48 hours. This lack of a single definition does not help pharmaceutical manufacturers and logistics providers when trying to ensure the GDP compliance of their supply chains.

So, three years on from the publication of the EU GDP, where should you be, in which direction should you be going, and how can you achieve compliance without massively increasing your logistics costs?

Risk Mitigation

If you take the risk-based approach, then route risk assessments are a good first step. These involve looking at all aspects of the path your product will take to market and understanding the potential temperature and quality challenges faced on the way.

The next step would be to temperature-map each route. This is where you carry out temperature logging of actual shipments by adding data loggers to map the conditions to which your products are exposed. In conjunction with route risk assessments and further analysis, this enables you to 'qualify' a route such that it can be used for shipments without further temperature measurement. In this respect, qualification means establishing confidence that the process is effective and reproducible.

However, this mapping may highlight temperature risks along the way, such as at a transit airport or a trucking hub. This knowledge will allow you to take risk mitigation action including the addition of thermal protection, or a switch to a specialist airfreight pharma service (where the airline offers additional thermal protection and special handling services) in order to maintain the label claim of your product. Equally, your route qualification could show you that no mitigation is required and that your shipments can continue as before. However, route qualifications should be done regularly or when there is a known change, like that of airport, logistics provider or mode of transport.

Air Shipment Options

One pharma manufacturer was able to identify the types of risk mitigation it would use for shipments by air for their different product groups (see Table 1). This will give you some idea of the choices available and when they may be deployed, although your own risk profile may differ significantly.

Active Containers

With sensors monitoring the temperature in order to adhere to the required conditions inside, active containers are highly effective.

More than half of the total flight time is actually spent on the ground and this is where the most common risks occur – mainly due to the wide variations in ambient temperature – but an active container will maintain the set temperature irrespective of the ambient conditions. Data monitoring and in-transit documentation ensure you can follow the exact status of your shipment anytime during the journey. This is typically the most expensive method of transporting products.

Airline Pharma Services

There are wide variations in airline pharma services' efficacy and offering. At the one end are those that have temperature-controlled warehouses and specially trained staff. Additionally, they use temperature-controlled trucks to deliver products to the aircraft with loading taking place as near to take-off as possible, thus minimising the 'tarmac time' when exposure to temperature can be high. At the receiving end, the reverse happens in order to offer maximum protection at all times. However, at the other end of the scale are airlines whose pharma service is merely a slightly quicker than normal service with no temperature-controlled facilities or special handling services. Prices vary but they are usually cheaper than active containers.

Passive Containers

These containers normally use phase change materials such as gel packs, which are pre-cooled to a defined temperature. The container is then built in a controlled environment and, once sealed, is validated to maintain the required temperature for 3-4 days. These provide excellent protection from rough handling and mean that products can go as general cargo,

thus saving a considerable sum of money over active containers or airline pharma services. However, correct training in the building of these containers is a must in order for them to perform to their designed capabilities.

Blankets
Offering a level of guarantee at a considerably reduced cost to all the other mitigating options mentioned, blankets are becoming the more popular choice. Technology and application differ, but the best seek to reflect external heat away from the product and lessen the risk of a temperature excursion during the times of highest exposure – such as on the tarmac during loading and unloading. Additional features can include breathability and protection from low temperatures.

No Protection
Surprisingly, Table 1 also shows that some products are still sent with no protection on a general cargo service, but a more stringent application of GDP through regulatory audits is likely to see a significant decline in this method.

Transport by Sea

Many manufacturers can, of course, choose to use seafreight as a transport mode. Typically this would involve lower value products, but that is changing and airfreight has dropped from carrying 17% of pharmaceuticals to 11%. Investigating this a little further shows that, by value, airfreight is responsible for 82% of products and seafreight only 18%; however, if we look at tonnage, the figures switch so that airfreight is now 13% and seafreight 87%. Thus, it is still generally true that high-value products go by air but in relatively small quantities, whereas large quantities of lower value products go by sea.

Seafreight is peculiar in that it is governed by old sets of rules such that the vessel liability can be extremely high. For this reason, many shipping lines have shied away from higher value pharmaceuticals, although the more enlightened are beginning to implement ways in which the pharma company can rid them of this high liability through indemnification.

> “Data monitoring and in-transit documentation ensure you can follow the exact status of your shipment anytime during the journey”

Temperature-controlled seafreight is achieved through the use of refrigerated containers, commonly known as reefers. Managed properly, these can be an excellent solution – but they require external power to operate, so there are known gaps in the supply chain. These would occur at ports during loading and unloading, or when the container is being unloaded from the truck, delivering it to port before it is then located in the reefer stack. The same will happen in reverse at the destination. Thermal blankets and passive packing units are being designed and deployed to mitigate these risks and have shown much success, but their use is variable.

Across Land

Of course, many shipments are continental, so do not use air or sea but travel by trucks. Trucks have become very sophisticated and the best operators will provide full track and trace so that you can see, in real time, where all your shipments are and the temperature they are experiencing.

No transport mode is immune from problems and, despite their advancement, trucks are no exception. These might include doors being opened and closed regularly during deliveries, products put in the wrong zone on bithermal trucks, or the temperature being erroneously set. Additionally, some companies persist in the use of non-temperature controlled trucks, which offer no protection from whatever the ambient climate conditions happen to be. Again, blankets are beginning to be utilised to mitigate the risk of a temperature excursion during transit, but this is also variable.

In summary, the transport of pharmaceuticals is no longer the straightforward exercise it used to be, but with the right partners and expertise, it can be done compliantly yet cost-effectively to the satisfaction of internal quality, logistics and finance departments, as well as external regulators.

About the author

Mark Edwards is Managing Director at Modalis, a pharmaceutical logistics consultancy. He has over 25 years of logistics experience garnered at a variety of logistics service providers and product manufacturers. Prior to Modalis, Mark served as Global Freight and Compliance Manager at Actavis, a top global pharma manufacturer. He was responsible for all aspects of international logistics and was the subject matter expert for transportation, warehousing, Incoterms, customs’ compliance, GDP and new product launches.
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