

## Temperature-controlled Distribution in the Healthcare Industry – A Field of Growing Importance

a report by

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According to John Taylor, a representative of the Quality Systems Division of the Medicines and Healthcare products Regulatory Agency (MHRA), around one-quarter of all significant failures to comply with good distribution practice are due to inadequate control and/or monitoring of storage and transportation temperatures. While temperature-controlled distribution has always been important to the healthcare industry, the current biotechnological revolution has further increased the need for the protection of thermally unstable products. At the same time, the healthcare supply chain is becoming more complex, with smaller and more frequent shipments further increasing the demand on solutions.

### Temperature-sensitive Products are Increasing in Importance

Although some observers believe that the rate of growth for the global healthcare industry will slow down considerably over the next few years, at the same time, they agree that some segments will sustain or increase growth rates. One such segment, which is growing faster than the industry in general, is the biotechnology segment. Of the more than 130 biotechnology drugs and vaccines approved by the US Food and Drug Administration (FDA), 70% were approved in the last six years.<sup>1</sup> At the same time, there are more than 350 biotechnology drug products and vaccines currently in clinical trials, targeting more than 200 diseases.<sup>1</sup> Many of these biotechnology drugs are temperature-sensitive. It is estimated that the temperature-sensitive segment is growing at a rate of about 15% per year.

### Demands on Temperature Control Solutions

Besides the basic requirement to keep the product temperature within set limits, a temperature control solution also has to fulfil other criteria. It has to be cost-effective with regard to the total cost of a given solution, such as packaging materials, carrier charges, handling costs and cost of rejected products. It also has to be compliant with regulatory demands, with

testing and validation reports as minimum steps to demonstrate that the temperature of products shipped will remain within the acceptable temperature range. Environmental aspects is an area that is becoming increasingly important for regulators. As such, it is also an area that has implications for the users of non-reusable distribution solutions.

The distribution chain is becoming more and more complex. A temperature control solution has to be in step with the increasingly complex demands of modern supply chain logistics. In its simplest version, the distribution chain may consist of only one shipment direct from the manufacturer to the end-user. However, more often, the distribution chain involves a number of transit locations and storage and handling by different parties. Smaller and more frequent shipments are becoming more usual.

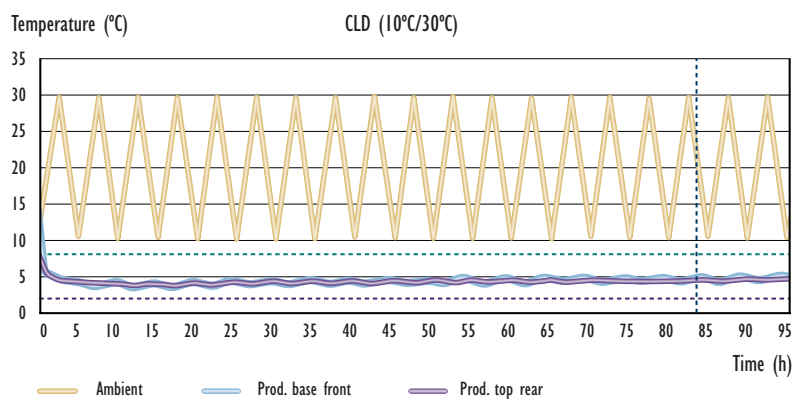
Storage and transportation temperatures are a highly significant factor in maintaining the quality of healthcare products throughout the distribution network. Standard operating procedures have to be in place to manage uncontrolled variables such as weather changes or delays due to trade union strikes.

### Alternative Solutions to Avoid Temperature-related Problems

To avoid temperature-related problems such as denatured proteins and a reduced shelf life, a wide array of packaging solutions have been used by the healthcare industry. The solutions consist mostly of insulating foam (usually expanded polystyrene or polyurethane) covered by a plastic layer. Gel packs and other phase change materials such as dry ice or wet ice have been used to maintain the temperature of these shippers. Although versatile and with the benefit of being easy to tailor for specific shipping requirements, disadvantages with these insulated shippers are: the amount of cooling medium needed due to its passive nature, which increases weight and volume and therefore air freight costs; and the amount of labour associated with the preparation of such a system prior to its utilisation.

1. *Biotechnology Industry Organization (2002).*

Figure 1: Validity Testing of the CLD Container



The graph shows that the CLD container kept the product temperature within set limits (+2°C to +8°C) for the required 84 hours as per the specification of the container.

During the mid-1990s, the air freight industry and specialists in the temperature-controlled logistics industry responded to the needs of the pharmaceutical industry by developing active temperature control solutions. As they are based on the configurations of standard air freight containers – known in the airline industry as unit load devices – the infrastructure at airports was already in place. In general, these temperature-controlled units are being used for healthcare products such as plasma, vaccines, interferons, blood fractions and diagnostics. The active temperature control technology uses dry ice as the temperature-controlling medium. The system is constructed from high-performance insulation material and comprises an internal fan and sensor. It works through a process of cooling warm air drawn in by the fan. The convection process promotes a constant, regulated environment.

### New Developments in Active Temperature Control Technology

While the active temperature control technology has had relatively few product volume constraints compared with conventional insulated passive systems, it has, until recently, had no alternatives for small-volume consignments. As a result of a major research effort focused on the logistical needs of the healthcare industry, a smaller unit, the Controlled Logistics Device (CLD), has been developed. It is designed specifically for small-volume shipments of healthcare products. The unit has been validated for shipments of 2–8°C, as well as for frozen products below -20°C.

The development process has benefited from the close exchange of ideas between the logistical solutions provider and the healthcare industry through the PharmaLogisticsForum initiated by Lufthansa Cargo and logistical managers of the healthcare industry in 2000. Envirotainer participated as a logistical solutions provider expert. The Forum has been involved in the development process, from the initial stages (with input

on the performance needed), to the final stages (with field tests to confirm that the unit acts as intended when exposed to a real transportation cycle).

Besides allowing active temperature control for smaller shipments, the unit delivers on the demand coming from an increasingly complex supply chain, and increases the logistical flexibility by allowing a pallet load to be broken up easily into smaller shipments, without compromising product integrity.

### Validity Testing of the CLD Container

The following example is one of the validity tests that the CLD container has undergone. The healthcare products chosen for this specific test were 0.5ml syringes with a density of 1.007kg/m<sup>3</sup>, placed in corrugated boxes that were then put in the container. The product was prepared with thermocouples and was then temperature-stabilised at +5°C for 24 hours. The preconditioning was verified by measuring the temperature of the goods.

The container was filled with the product load and 16 new alkaline batteries were installed. The thermostat was set to the required temperature of 5°C. Wrapped ice was then distributed evenly in the dry-ice bunker, and the loaded container was placed inside an environmental test chamber. The temperatures of the ambient and the pharmaceutical product were recorded at two-minute intervals. In this specific test, the ambient temperature was ramped between +10°C and +30°C. The duration of the test was 84 hours to test the performance of the container. The container kept the product temperature within the set limits (+2–8°C) for the required 84 hours, as per the specification of the container (see Figure 1).

The first commercial use of the container took place in November 2002 and involved a shipment from Switzerland to Japan. It has since been used successfully in more and more shipments, demonstrating the viability of the concept.

### Conclusion

This current trend is likely to continue, with the growth of the biotechnology sector being one of the key drivers. This development is increasing the need for temperature control solutions in general. At the same time, the need for standardised distribution solutions, allowing smaller shipments, is increasing as the healthcare supply chain continues to become more and more complex. With the advent and continued advancement of active temperature control technology, the logistics industry, together with logistical representatives of the healthcare industry, has created a solution that addresses these issues successfully. ■