The importance of good distribution practice

Historically, the regulation and control of medicinal products has relied on national and supranational guidelines covering good manufacturing practice (GMP). However, the quality of these medicinal products can be adversely affected by a lack of adequate control over the myriad activities that occur during the distribution process. In addition, the necessity for developing, establishing and maintaining an adequate control system has not generally been well understood. This may result in differences in documentation practices and handling requirements, as well as communication between the various organisations, companies, groups or entities that comprise the supply chain.

This is where good distribution practice (GDP) comes in. The US Pharmacopeial Convention believes that GDP should “facilitate the movements of drug products throughout a supply chain”, while the European Medicines Agency has stated that GDP ensures “the level of quality determined by GMP is maintained throughout the distribution network, so that authorised medicines are distributed to retail pharmacists and others selling medicines to the general public without any alteration of their properties.”

Like GMP, GDP is regulated and controlled by numerous national and supranational guidelines. It is reliant on a series of inter-connecting quality systems operated by wholesalers or distributors of pharmaceutical drug products. The systems ensure the following: distributed products are authorised in accordance with the relevant legislation; appropriate storage conditions are maintained at all times, including movement of goods between various parts of the distribution network; contamination by other products is avoided; an appropriate turnover of stock takes place; and that products throughout the distribution chain are stored in safe and secure areas. In addition, to help combat counterfeiting, there should be a system(s) to enable faulty products to be rapidly found and recalled. In parallel, an effective quality system is required to ensure that the right product is delivered to the right location within a designated time period.

Those GDP issues that affect product quality are similar to those bedevilling GMP, that is, errors (mix-ups), contamination and cross-contamination. However, inadequate or inappropriate storage conditions, as well as supply chain security considerations (counterfeiting or adulteration) are also important. Therefore, all organisations that are part of the supply chain have a shared responsibility for ensuring that they transport/store drug products under appropriately controlled conditions that will not affect drug product quality, efficacy or safety and that they pass the drug product onto the next part of the supply chain in an appropriate manner.

One of the most important considerations of GDP is therefore storage and shipping. Each organisation is required to define and control appropriate facilities, which include those which receive, hold and transfer the product. It is thus important that drug products should be continuously monitored and verified by appropriately calibrated monitoring systems or that the supply chain is appropriately qualified based on historical data.

However, it may be acceptable to use a combination of drug product stability data and supply chain risk assessments to justify shipping products without continuous verification of supply chain qualification. One of the most important considerations in the latter approach is to assess the impact of temperature excursions, i.e., those parts of the supply chain where temperature is not effectively controlled within pre-defined ranges. This can be accomplished using mean kinetic temperature (MKT). MKT can be considered as ‘an isothermal temperature that stimulates the non-isothermal effects of storage temperature deviation’.

The MKT calculation is therefore deemed to be an appropriate approach to justify temperature excursions that occur during transit, but the MKT calculation must be justified by ensuring that the drug product follows first order kinetics over the temperature range encountered. That is, that product exposed to temperatures of 80°C for 1 week will follow the same degradation pathway as product exposed to temperatures of 40°C for 6 months.

In summary, complex multinational supply chains for pharmaceutical products are increasingly becoming the global norm. Against this background GDP is an essential practice to ensure the continuing quality of medicinal products. However, the resultant supply chain is only as strong as the weakest part and it necessitates the combined efforts of all parties to ensure the continued success of GDP and thereby the continued assurance of product quality.

References
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2. USP <12079> Good storage and distribution practices for drug products. 2015