Whitehall Training

Good Distribution Practice (GDP)

What is Good Distribution Practice?

The aim of **Good Distribution Practice (GDP)** is to maintain the integrity of medicinal products during transport and storage stages of the drug manufacture and distribution process.

GDP is partially about ensuring that products reach the end-user in as good a condition as they left the manufacturer. The other aspect of GDP is ensuring that products are what they appear to be - that the supply chain is protected from counterfeits and that genuine products have not been tampered with.

Whilst GDP is not concerned with product manufacturing processes, it does provide another check on packaging and labelling. Because of this, GDP can be seen as a sub-set of Good Manufacturing Practice (GMP).

Where did GDP come from?

In 1937, 107 people died when diethylene glycol was incorrectly used in the manufacture of a liquid form of the drug, elixir sulphanilamide. The company involved was fined the largest fine ever and the tragedy prompted development of better methods for determining toxicity.

In 1941, sulfathiazole tablets were found to be contaminated with phenobarbital. Nearly 300 people died as a result and the subsequent investigation and product recall attempts showed up serious deficiencies and irregularities in the manufacturer's activities. This prompted the FDA to require detailed production controls, which became the basis for modern production control standards.

In 1978, the US finalised its Good Manufacturing Practices (GMPs) for drugs and medical devices, establishing a minimum standard for manufacturing, processing, packing, or holding drug products and medical devices.

Since then, GDP rules have been adopted globally and are being regularly revised to accommodate new manufacturing process, and drug formulations. They also need to adapt to respond to the increasingly sophisticated counterfeit drug trade.

Organisation, Personnel & Responsibilities

Licensed distributors must ensure that -

- The drug is being used in a controlled environment
- GDP is followed and an appropriate Quality System is in place
- Product supply is maintained, as far as possible
- Products are only supplied through lawful means, under valid marketing authorisations (MAs) and using authorised suppliers, to those also authorised to deal with them
- Staff, premises and equipment are appropriate to the activities being performed
- There is a nominated individual with responsibility for ensuring a quality system is implemented and maintained.
- Written procedures are in place for any operations that may affect product quality
- Appropriate records are maintained under the quality system
- An emergency plan is in place to ensure effective recall of product from the market
- The quality and integrity of the product is maintained.

The Responsible Person (RP)

Under Directive 2001/83/EC, holders of a distribution authorisation must have a "qualified person designated as responsible." In the UK, under the Medicines for Human Use (Manufacturing, Wholesale dealing & Miscellaneous Amendments) Regulations 2005, this person is known as the "Responsible Person" or RP.

The RP should ensure that the conditions of the wholesale dealer's licence are being met and that GDP is being followed. If they do not carry out those duties well enough then the licence can be suspended and the acceptability of that person as an RP may be withdrawn.

Other key staff

Depending on the size of the organisation, there may be any number of additional staff involved in operations, such as warehouse staff, drivers and administrative staff. There must be an organisational chart, clearly indicating the responsibilities, roles and interrelationships of all personnel.

All staff involved must understand the importance GDP and how their role and activities fit into the picture. Lack of training, inadequate training, or training on out of date requirements, are a root cause of many problems encountered in the GDP environment.

Facilities and Equipment

Premises and equipment should be suitable and adequate to ensure proper conservation and distribution of medicinal products. The premises should be designed or adapted to be suitably secure and structurally sound. They should be kept clean, dry and within acceptable temperature limits.

Receipt of Goods

Delivery bays should protect deliveries from bad weather during unloading. The reception area should be clearly designated and should be separate from storage and dispatch areas so it is clear which stage of processing goods are in at any given time.

Deliveries should be examined on receipt to ensure that containers are not damaged, that goods have not been tampered with, and that the consignment matches the order.

Storage

Medicinal products should be stored apart from other goods, under the conditions specified by the manufacturer. The storage facilities should be clean and free from dust, litter and pests. Adequate precautions should be taken against spillage, breakage, attack by micro-organisms and cross-contamination.

There should be separate areas designated for "quarantined" goods, i.e. returned goods, suspected falsified or counterfeit goods, expired or rejected product, products awaiting disposal or recalled products.

The temperature of the storage facilities should be monitored and recorded periodically. The records of temperature should be reviewed regularly as part of the quality system. When specific temperature storage conditions are required, the storage areas should be equipped with temperature recorders or devices that will indicate that the correct temperature range has been maintained.

Alarm levels should be appropriately set and alarms should be tested to ensure they work effectively.

Temperature mapping should be performed to examine the accuracy of storage temperatures in cold storage. This involves placing temperature probes or recording devices at appropriate places in the storage area and monitoring the temperature over time.

Current UK guidance requires mapping of internal air temperature distribution on installation in the empty and full state and annually thereafter under normal conditions of use.

Paperwork

Sales Orders

Sales orders are one of the most obvious sets of documentation involved in distribution activities. It is essential that records of sales are kept and maintained so as to preserve traceability of all products handled. There should be clear records of all deliveries to customers and for all supplies, a document must be enclosed that makes it possible to tell details like batch number, storage conditions and name and address of supplier.

Receipt of Goods

Deliveries from wholesalers should only be made to those persons who are authorised to handle them. This means other authorised wholesalers or those authorised to supply medicinal products to the public.

This process of checking the validity of customers' authorisations should be documented. Additional checks should be carried out with new suppliers to assess their suitability, competence and reliability.

Standard Operating Procedures

One of the key elements of any Quality Management System (QMS) is written documentation that sets out how processes and procedures are to happen. These must be accessible to those who need to use them and they should be part of a document control system, which ensures they remain up to date and accurate. Most of the industry refers to them as standard operating procedures (SOPs) but they can also be known as work instructions or standard procedures etc.

SOPs must be written in clear unambiguous language, set at a comprehension level appropriate to those who will be trained in, and using, the procedure. SOPs should include not only clear instructions for the activities to be undertaken but also indicate responsibilities for those activities, including management responsibilities.

Records

This is probably the largest body of documentation. It includes any recorded information or data that builds up the picture of compliance and quality management for the storage and distribution of medicinal products.

Information and data should be recorded at time the actions are performed. Records should be taken and kept in a way that all significant activities or events are traceable.

All documentation should be readily available and should be made available on request by the competent authorities.

Documents should be retained for a period stated in the national legislation but at least 5 years.

Distribution

The specified conditions for storing medicinal products must be observed at all times, including during transportation. Products should be transported in a way such that -

- Identification is not lost
- Products cannot contaminate or be contaminated by other products or materials
- Products are adequately protected from spillage, breakage, theft, extreme conditions and from attack by micro-organisms and pests

Orders should be picked and packed so that the correct goods are picked with appropriate remaining shelf life and the packing maintains the storage conditions of the product during transport, as well as physically protecting the goods.

Containers in which medicinal products are shipped should be sealed and exhibit clear labelling regarding the handling and storage conditions and allow ease of identification of the product inside.

Transport Methods

Appropriate transport methods should be used for each shipment and these may be any, or a combination, of air, road, sea or rail. Some modes of transport may not be appropriate for a particular shipment, for example for radioactive or temperature-sensitive substances. Regardless of the method used, it should be possible to demonstrate that the products have not been subjected to conditions that might compromise their quality or integrity.

Complaints & Returns

Written procedures should be in place for dealing with complaints and returns, particularly focusing on handling potentially defective products. Such documentation should indicate who has responsibility for handling complaints.

Records should be kept regarding any returns or rejections and their ultimate disposition. All handling of returned medicinal products including their return to saleable stock or disposal should be approved by the RP.

Product Recalls

Recalls and alerts for action are normally issued by the authorities and/or MAH (marketing authorisation holder) and are given different levels of priority for action depending on the nature, severity and impact of the problem. The messages issued provide detail of the product, the action required and the timeframe in which action must be taken, and the wording is normally mutually agreed between the authorities and the company.

Counterfeit Products

The Falsified Medicines Directive (FMD)

The Falsified Medicines Directive (Directive 2011/62/EU) introduced pan-European rules to improve the protection of public health by ensuring that medicines are safe and that the trade in medicines is rigorously controlled. To achieve this, the Directive requires -

- Obligatory safety features on the outer packaging of the medicines
- A common, EU-wide logo to identify legal online pharmacies
- Tougher rules on the controls and inspections of producers of active pharmaceutical ingredients
- Stronger record-keeping requirements for wholesalers.

The US Drug Quality and Security Act

Since 2017, all medicine packages in the US have been required to carry serial numbers. By 2023, the packages should use electronic codes.

A standardised "track and trace" programme would remove inconsistencies from current state-by-state measures, such as California's planned electronic labelling requirements. It also standardises the rules that must be followed by manufacturers and compounders.

Previously, pharmacies were regulated at state level as opposed to drug manufacturers who are regulated by the FDA. Compounding pharmacies will be able to register with and be inspected by the FDA, allowing the FDA to track their products alongside those from drug manufacturers.

Training

The quality of falsified goods varies, but many are very accurate copies of the original product. All personnel involved in distribution must be aware of the risks of falsified goods entering the supply chain and receive training to look out for indicators that medicinal products may not be genuine.

Whitehall Training

This is the end of Whitehall Training's short **GDP** course.

Expanded online versions of this training, complete with exam and certificate, are available from the Whitehall Training website – **https://www.whitehalltraining.com/good-distribution-practice-courses**