New Guidelines on Good Distribution Practice of Medicinal Products for Human Use
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Topics

• GDP format and date for adoption.
• Key new areas covered by the GDP Guide
Background

The EU Commission have revised the Guidelines on Good Distribution Practice to update them to reflect more complex supply chains of the 21st Century.

The new GDP was published on 7 March 2013 and will be adopted as the required standard for Wholesale Distributors 6 months later.

The existing guide was in place for 19 years and many of the requirements had been expanded in additional national guidance. These slides highlight the areas that have never previously been required or expected of UK wholesalers.
Chapter 1 Quality Management

“Wholesale distributors must maintain a quality system setting out responsibilities, processes and risk management principles in relation to their activities. All distribution activities should be clearly defined and systematically reviewed. All critical steps of distribution processes and significant changes should be justified and where relevant validated. The quality system is the responsibility of the organisation’s management and requires their leadership and active participation and should be supported by staff commitment.”

An increased emphasis on the quality system setting out in detail additional expectations on how the QMS should operate. For companies operating ISO QMS this should already be in place. Significant impact for smaller wholesalers where basic SOPs are the accepted norm.

Key new areas:
• Change control,
• CAPA
• Quality Risk Management
Management Review and Monitoring
“The management should have a formal process for reviewing the quality system on a periodic basis. The review should include:

i) Measurement of achievement of quality system objectives;
ii) Assessment of performance indicators that can be used to monitor the effectiveness of processes within the quality system, such as complaints, deviations, CAPA, changes to processes; feedback on outsourced activities; self assessment processes including risk assessments and audits; external assessments such as inspections, findings and customer audits;
iii) Emerging regulations, guidance and quality issues that can impact the quality management system;
iv) Innovations that might enhance the quality system;
v) Changes in business environment and objectives.”

The outcome of each management review of the quality system should be documented in a timely manner and effectively communicated internally.
Chapter 1 Quality Management

Quality Risk Management

“Quality risk management is a systematic process for the assessment, control, communication and review of risks to the quality of medicinal products. It can be applied both proactively and retrospectively.”

Quality risk management should ensure that the evaluation of the risk to quality is based on scientific knowledge, experience with the process and ultimately links to the protection of the patient.

The level of effort, formality and documentation of the process should be commensurate with the level of risk.
Chapter 2 Personnel

“The correct distribution of medicinal products relies upon people. For this reason, there must be sufficient competent personnel to carry out all the tasks for which the wholesale distributor is responsible. Individual responsibility should be clearly understood by the staff and be recorded.”

Sets out in detail the role of the Responsible Person, the need for organisational charts, job descriptions the expectations on staff training and hygiene.

Key new areas:

• The Responsible Person should fulfil his responsibilities personally and should be continuously contactable. The responsible person may delegate duties but not responsibilities.
• Requirement that staff are trained in GDP and that the RP has regular training.
• A requirement for personnel hygiene to be considered.
Chapter 3 Premises and Equipment

“Wholesale distributors must have suitable and adequate premises, installations and equipment, so as to ensure proper storage and distribution of medicinal products. In particular, they should be clean, dry and maintained within acceptable temperature limits.”

A significant expansion on the details of the premises, setting out in detail temperature mapping requirements, the use of electronic systems to segregate stock and qualification and validation of equipment.

Key new areas:
• Records to be kept of repair, maintenance and calibration of key equipment.
• Validation of computer systems.
• Qualification and validation of key equipment.
Chapter 3 Premises and Equipment

*Computerised Systems*

“Before a computerised system is brought into use, it should be demonstrated through appropriate validation or verification studies, that the system is capable of achieving the desired results accurately, consistently and reproducibly.

- A written detailed description of the system should be available (including diagrams where appropriate). This should be kept up-to-date. The document should describe the principles, objectives, security measures, system scope and main features and how the computerised system is used and the way it interacts with other systems.
- Data should only be entered into the computerised system or amended by persons authorised to do so.
- Data should be secured by physical or electronic means and protected against accidental or un-authorised modifications. Stored data should be checked periodically for accessibility. Data should be protected by backing up at regular interval.
- Back up data should be retained for the period stated in national legislation but at least 5 years at a separate and secure location. Procedures to be followed if the system fails or breaks down should be defined. This should include systems for the restoration of data.”
Qualification and Validation

“Wholesale distributors should identify what key equipment qualification and/or key process validation is necessary to ensure correct installation and operation. The scope and extent of such qualification and/or validation activities (such as storage, pick and pack processes) should be determined by a documented risk assessment approach.

- Equipment and processes should be respectively qualified and/or validated before commencing use and after any significant changes e.g. repair or maintenance.
- Validation and qualification reports should be prepared summarizing the results obtained and commenting on any observed deviations. Deviations from established procedures should be documented and further actions decided to correct deviations and avoid their reoccurrence (corrective and preventive actions). The principles of CAPA should be applied where necessary. Evidence of satisfactory validation and acceptance of a process or piece of equipment should be produced and approved by appropriate personnel.”
“Good documentation constitutes an essential part of the quality system. Written documentation should prevent errors from spoken communication and permits the tracking of relevant operations during the distribution of medicinal products”

Defines documentation as all written procedures, instructions, contracts, records and data, in paper or in electronic form. An expansion on how documents should be managed and controlled.

Key new areas:
• The documentation should be in language understood by the personnel
• Version control for procedures and emphasis on ensuring documentation is up to date
Chapter 5 Operations

“All actions taken by wholesale distributors should ensure that the identity of the medicinal product is not lost and that the wholesale distribution of medicinal products is performed according to the information on the outer packaging. The wholesale distributor should use all means available to minimise the risk of falsified medicinal products entering the legal supply chain.”

A significant expansion on the details on checking the bona fides of suppliers and customers and the introduction of due diligence. Export is now covered by GDP.

Key new areas:
- Verifying the supplier is compliant with GDP
- Due diligence checks on the supplier
- Monitoring sales to identify misuse or diversion of medicines
- Requirement for a control report when sourcing goods from EEA States
- Requirement for First Expiry First out, rather than FIFO
- Stock inventories should be performed regularly
- Exporting medicines out of the EEA requires a wholesale authorisation and full GDP is applied
Chapter 6 Complaints, Returns, suspected falsified Medicinal Products and Medicinal Product Recalls

“All complaints, returns, suspected falsified medicinal products and recalls must be recorded and handled carefully according to written procedures. Records should be made available to the competent authorities. An assessment of returned medicinal product should be performed before any approval for resale. A consistent approach amongst all partners within the supply chain is required in order to be successful in the fight against falsified medicinal products.”

No significant changes to current requirements.

The new guide suggests 10 days may be an acceptable time limit to return medicines that have been outside the Licensed chain. MHRA will maintain its existing guidance on the acceptance of returns to saleable stock.

Stolen medicines that are recovered cannot be returned to saleable stock.
Chapter 7 Outsourced activities

“Any activity covered by the GDP Guide that is outsourced should be correctly defined, agreed and controlled in order to avoid misunderstandings which could affect the integrity of the product. There must be a written Contract between the Contract Giver and the Contract Acceptor which clearly establishes the duties of each party.”

A full set of requirements for contracts between parties where GDP has been outsourced. These match current MHRA expectations. Contracted out activities should be audited as part of management review.

Audits by independent external experts may also be useful but may not be used as a substitute for self-inspection.
Chapter 8 Self-Inspections

“Self-inspections should be conducted in order to monitor the implementation and compliance with GDP principles and to propose necessary corrective measures.”

An expansion of how self inspections are to be conducted and recorded.

Key new areas:
• Self inspections can be carried out by staff other than RP. An independent external audit is recommended.
• The reports should be subject to CAPA principles
Chapter 9 Transportation

“It is the responsibility of the supplying wholesale distributor to protect medicinal products against breakage, adulteration and theft, and to ensure that temperature conditions are maintained within acceptable limits during transport. Regardless of the mode of transport, it should be possible to demonstrate that the medicines have not been exposed to conditions that may compromise their quality and integrity. A risk based approach should be utilised when planning transportation.”

A significant expansion on the requirements to control distribution. An emphasis that products should be shipped according to the labelled conditions and that excursions are reported. There are detailed requirements for shipping temperature sensitive items. Contracted transporters should be informed of storage conditions

Key new areas:
• Medicines to be shipped within label conditions
• Temperature excursions should be reported and investigated
• Risk assessments of delivery routes to identify when temperature control is needed.
• Dedicated vehicles to be used where possible. Procedures to cover use of non dedicated vehicles.
• A contract to be in place with transporters as required by Chapter 7.
Chapter 9 Transportation

“The required storage conditions for medicinal products should be maintained during transportation within the defined limits as described by the manufacturers or on the outer packaging.

- If a deviation such as temperature excursion or product damage has occurred during transportation, this should be reported to the distributor and recipient of the affected medicinal products. A procedure should also be in place for investigating and handling temperature excursions.

- Risk assessment of delivery routes should be used to determine where temperature controls are required. Equipment used for temperature monitoring during transport within vehicles and/or containers, should be maintained and calibrated at regular intervals at least once a year.

- Dedicated vehicles and equipment should be used, where possible, when handling medicinal products. Where non-dedicated vehicles and equipment are used procedures should be in place to ensure that the quality of the medicinal product will not be compromised.

- Where transportation is performed by a third party, the contract in place should encompass the requirements of Chapter 7. Transporters should be made aware by the wholesale distributor of the relevant transport conditions applicable to the consignment. Where the transportation route includes unloading and reloading or transit storage at a transportation hub, particular attention should be paid to temperature monitoring, cleanliness and the security of any intermediate storage facilities.

- Provision should be made to minimise the duration of temporary storage while awaiting the next stage of the transportation route.”

“Containers should bear labels providing sufficient information on handling and storage requirements and precautions to ensure that the products are properly handled and secured at all times. The containers should enable identification of the contents of the containers and the source.”
Chapter 10 Specific Provisions for Brokers

“A "Broker" is a person involved in activities in relation to the sale or purchase of medicinal products, except for wholesale distribution, that do not include physical handling and that consist of negotiating independently and on behalf of another legal or natural person. Brokers are subject to a registration requirement. They must have a permanent address and contact details in the Member State where they are registered. They shall notify the competent authority of any changes thereof without unnecessary delay. By definition, brokers do not procure, supply or hold medicines. Therefore, requirements for premises, installations and equipment as set out in Directive 2001/83/EC do not apply. However, all other rules in Directive 2001/83/EC that apply to wholesale distributors also apply to brokers.”

Sets out the requirements for records and procedures required for brokers. This is a new area not previously required.
Definitions

The final annex provides a glossary of terms
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