ECA Roadmap to Good Distribution Practice (GDP)

EU Guidelines on Good Distribution Practice (2013/C 343/01)

The European GDP Association has compiled this document to support pharmaceutical and wholesaler businesses in implementing regulatory requirements and expectations in their quality systems.

In addition it provides checklists to verify the minimum implementation of GDP.

Regulatory References:

- Guidelines on Good Distribution Practice of Medicinal Products for Human Use (2013/C 343/01)

Background:

The European Commission's Directorate General for Health and Consumer Policy (DG SANCO) published the final version of the 'Guideline on Good Distribution Practice of Medicinal Products for Human Use' on 05 November 2013.

These 2013 guidelines revised the previous 1994 version to take into account advancements of practices for appropriate storage and distribution of medicinal products within the European Union. The updates introduced the requirement for brokers of medicines to ensure their practice is aligned to the guidelines. There is also specific guidance to wholesalers and their appointed Responsible Person (RP). Moreover, the 2013 guidelines take into account the amendments to the Community Code which have been introduced with Directive 2011/62/EU of the European Parliament and of the Council amending Directive 2001/83/EC on the Community code relating to medicinal products for human use, as regards the prevention of the entry into the legal supply chain of falsified medicinal products.

This Roadmap to GDP provides the following:

1. An outline of the GDP Chapters
2. A Dedicated Responsibilities matrix*
3. A GDP Checklist for Wholesale Distributors*

*This matrix pulls out relevant responsibilities from the guidelines; note each specific organisation should add to this in line with their operations and requirements on the RP and Management. The Checklist provides a generic overview and could be used as a minimum requirement from which organisation's can tailor suitable checklists for local use.

Chapter Outlines

Chapter 1 – Quality Management

The 2013 guidelines introduced the concept of **Quality Management** for wholesalers' which includes the principles of quality **risk management**. "*Wholesale distributors must maintain a quality system setting out responsibilities, processes and risk management measures in relation to their activities.*"
The organisation's management is responsible for the quality system, which requires their leadership and active participation supported by staff commitment. The Responsible Person is to ensure that a **Quality Management System** is implemented and maintained. The Management is to ensure that all parts of the quality system are documented, defined and are adequately resourced with competent personnel, and suitable and sufficient premises, equipment and facilities.

The **Quality System** should also define the organisation's

- **change control process**
- management of their **outsourced activities** with a clear requirement to assess the suitability of the Contract Acceptor to perform the required activities
- the formal process for **reviewing the quality management system** on a periodic basis (**Management Review**).

All significant changes should be justified, validated and approved by relevant stakeholders via change control and risk management processes, using appropriate corrective actions and preventive actions (CAPA).

Chapter 2 – Personnel

This chapter defines the qualification requirements, tasks and responsibilities of all staff and the Responsible Person (RP).

- This Responsible Person, RP, should be continuously contactable and perform his responsibilities personally.
- An RP can delegate his duties but not his responsibilities.
- The **RP Job Description** should clearly define their **authority to take decisions with regard to their responsibilities**.
- The RP should perform their duties ensuring their organisation can demonstrate compliance to GDP.
- Equally the RP's management is responsible for effectively resourcing and supporting the RP to fulfill their duties in line with their RP responsibilities.
- Specific duties of an RP have been described, which includes ensuring compliance with the authorised activities, ensuring initial and continuous training programs are implemented and maintained as well as the RP's decision-making responsibility, e.g. for disposition of returned and recalled products as well as approval of any subcontracted activity.

Training requirements for all staff including the RP are defined, there is a need for up to date

training records, staff should receive training on tasks they perform, products they handle and the GDP guidelines. The **practical effectiveness of training** should then be periodically assessed and documented for all staff.

Chapter 3 – Premises and Equipment

Premises should be designed and equipped so as to afford protection against the entry of insects, rodents or other animals. A preventative pest control program should be in place. The guidelines also require the rest areas, wash and refreshment rooms for employees to be adequately separated from the storage areas, and the presence of food, drink, smoking material or medicinal products for personal use should be prohibited in the storage areas.

Access to medicinal product storage areas should be restricted and monitored with procedures in place to prevent unauthorised access at all times, this includes preventing unauthorised access to computerised systems and documentation.

Requirements have been set for products with specific handling instructions, to be followed as specified in national law. For example narcotics, radioactive materials and other hazardous products as well as products presenting special risks of fire or explosion.
Premises and Equipment includes greater details. For example, it states "Products *pending a decision as to their disposition or products that have been removed from saleable stock should be segregated either physically or through an equivalent electronic system*". However, the clear requirement for **physical segregation** has been emphasised for the following

- recalled
- falsified
- expired
- rejected products
- products received from third countries and not intended for the Union markets

Initial **temperature mapping** of warehouses before use under representative conditions is required. After an initial mapping, temperature monitoring should be located according to the results of the mapping exercise. Mapping should be repeated according to the results of Risk Assessment and whenever significant modifications are made to the facility or temperature controlling equipment.

There is a focus on **equipment** and **computerised systems**, in that "*All equipment impacting on storage and distribution should be designed, located, maintained to a standard suitable to its intended purpose*". Annual calibration, with calibration certificates to be retained of monitoring devices, is now required. Calibration certificates should be available for the source equipment used to perform calibration which should be traceable to a national or international measurement standard. Equipment and computer alarm alerts should be set at appropriate levels to ensure product integrity can be maintained and the systems should be tested for accuracy and functionality.

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. Validation studies should support the system in use and

any significant changes should be validated prior to implementation. All data should be retrievable as required in national legislation but at least for a period of 5 years. The quality management system should define the procedures to follow if the computerised system fails or breaks down and how the data will be restored.

Key equipment and key processes should be identified for qualification and/or validation to ensure correct installation and operations. A written **risk assessment** should be used to determine the scope and extent of the qualification and/or validation noting the knock on effect into other areas which will require additional risk assessment and **risk management principles** to be applied.

Chapter 4 – Documentation

A good Quality Management System will be underlined by good documentation practice. Documentation comprises all written procedures, instructions, contracts, records and data, i.e. all information required to demonstrate the what, by who, when, how and why should be documented in the Quality Management System paying attention to compliance to Data Integrity, Data Management and Data Retention.

- The detail within documentation should be comprehensive, clear, concise and an accurate reflection of the organisation's policies, procedures, activities and its controls.
- Documents in foreign languages should be notarised to local languages.
- All documentation should be reviewed by persons with adequate knowledge of the task(s)
- Records should be completed at the time of the operation being performed.
- Changes should go through **Version Control** with significant changes being put through **Change Control** and where required **Risk Assessment and Risk Management**.

RP approval should be sought where required. All documentation whether current, superseded or withdrawn should be retained in line with national legislation but for a minimum of 5 years, document control logs should be made available for traceability and monitoring.

Chapter 5 – Operations

Qualification of Suppliers and Customers

All suppliers must be **qualified** in an adequate way, i.e. **wholesale distributors must verify** their

- **supplier** is *authorised to supply* medicinal products by way of wholesale dealing
- **customers** are *authorised to purchase* medicinal products either by way of wholesale dealing or as the authorised or entitled entity to receive and/or supply medicines to the public e.g. hospital, pharmacy, prison, university, research facility.

It is important that the qualification is performed prior to any procurement and any supply activities are authorised to take place. The selection, including qualification and approval of suppliers and customers should be defined in Standard Operating Procedures, SOPs, and the results should be documented and periodically evaluated.

Qualification is not a new requirement however, it emphasises the importance of preventing falsified medicine being supplied through authorised channels, and the need for periodic review of these authorisations has been defined.

Other requirements include the need for keeping records of all destroyed medicinal products for a defined period; again, it is not clear if this needs to be batch specific.

The export of medicinal products to third countries falls within the definition of 'wholesale distribution'.

Receipts of medicinal products, Storage and Destruction

Upon receipt, medicinal product should be visually inspected at Goods-In/Goods-Receipt area to ensure product is free from damage, tampering, contamination from other products and/or ingress of pests/dirt.

Products and documentation should be inspected for authenticity and accuracy on receipt. Anomalies should be documented and reported to the RP and Management according to written procedures. Products with special handling instructions should be processed first.

Medicinal product should be stored separately to other goods if the warehouse facility has multiple storage uses. Storage facilities should be clearly and adequately labeled to accurately identify stock. Stock should be stored according to the manufacturer's instructions and following national legal requirements e.g. narcotics, psychotropics, substances liable to misuse and hazardous goods.

Batches/products should be appropriately segregated to prevent cross-contamination and prevent inadvertent supply. This includes medicinal product held in quarantine or held for destruction. In both instances stock should be physically segregated, appropriately identified and handled in accordance with written procedures.

Picking, Supply and Export to Third Countries

Procedures should be written in a clear and concise language to be understood by the operators to ensure the correct product is picked for supply and has an appropriate shelf-life remaining.

A delivery document is required to be enclosed within all consignments containing complete product descriptions, quantities and information necessary to identify the supplier and consignee, along with any special handling and/or storage conditions.

Product intended for non-EEA countries falls under "Export" and as such the exporter must hold a wholesale distribution authrorisation or a manufacturing authorization permitting Export of medicinal products. The onus remains on the supplier to qualify their customer as entitled to receive the exported product.

Chapter 6 – Complaints, Returns, Suspected Medicinal Products and Medicinal product Recall

A complaints procedure should be in place which clearly defines the process steps for handling complaints received from customers. Complaints relating to distribution activities should be recorded, investigated to identify the root cause and where appropriate a corrective action to be identified. Product quality complaints should be forwarded to the manufacturer/MA holder for investigation.

Only the RP can authorise the final disposition of stock affected by a deviation, return, rejection or being suspected of being falsified or under a recall notice.

The major requirement in this section is to **immediately inform the competent authority and the marketing authorisation holder of any medicinal products identified as falsified or suspected to be falsified**. A procedure should be in place to cover this activity, including the recording of the relevant investigation.

Chapter 7 – Outsourced Activities

Clearly defines the roles and responsibilities of the Contract Giver and the Contract Acceptor and states the need for a detailed contract to cover the outsourced activity.
The Contract Giver is responsible for performing due diligence activities and, where required, to carry out an audit of the Contract Acceptor. Where a desk-top audit takes place full justification is required to be documented for not performing a physical audit.

Any work entrusted to the Contract Acceptor should not be outsourced to a third party without both an agreement from the Contract Giver and an audit of the third party.

Outsourced activities include for example:

- Storage at third party facility
- Transportation
- Equipment Calibration and Maintenance
- Pest Control
- Alarms and/or Security
- Cleaning and Facility Maintenance and Site Management

Chapter 8 – Self Inspections

This chapter defines the need for a Self-Inspection program, reporting of the findings and developing and implementing of appropriate CAPAs. The RP is responsible to ensure this program is maintained and thus is responsible for keeping up to date with changes in legislation and regulations impacting the business with regards to GDP. Other departments may support the RP by performing local audits and/or participating in the organisation's Self Inspection program.

Chapter 9 – Transportation

This is the most extensively developed addition to the 2013 GDP guidelines. It states that "*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 packing*".

Provisions should be made to minimise the duration of temporary storage (use of transport hubs) while awaiting the next stage of the transportation route.

There is emphasis on the responsibility of the distributors to ensure that vehicles (and equipment) used to distribute and transport medicinal products are suitable for their use *and* do not affect the quality of the product nor the integrity of packaging. This requires the distributor to audit their transport providers and thus there is an onus on transport providers to ensure their vehicles and drivers meet the expectations of GDP for medicinal products. The transport provider should have written procedures in place, and a Contract should be in place with the wholesale distributor clearly defining responsibilities.

Other additions include

- The requirement for procedures to be in place for the operation and maintenance of all vehicles and equipment involved in the distribution process.
- Risk assessment of delivery routes should be used to determine where temperature controls are required. They can also be used to determine optimum delivery times e.g. late night transport in summer months or specific months to avoid risk of adverse weather conditions delaying deliveries and/or compromising the vehicle or product packaging.
- Deliveries should be made directly to the address stated on the delivery note and must be handed into the care of the consignee using dedicated vehicles where possible.
- Medicinal products should not be left on alternative premises.
- Transportation performed by third parties should be covered by a contract (Chapter 7).
- Minimise the duration of temporary storage e.g. at hubs, while product awaits uplift or onward transshipment during delivery to the end customer.

Containers, packaging and labeling

The identity, integrity and quality of product should not be compromised by containers used to carry the goods, i.e. product should be appropriately packaged, clearly labeled and be protected from external influences and be free from risk of contamination.

Products requiring special conditions

The responsibility is on the wholesaler and transport/delivery provider to ensure a safe and secure supply chain is maintained for all medicinal products with special attention to products such as narcotics and psychotropic agents, in line with national legal requirements.

Products containing highly active and radioactive materials should be transported safely within secure containers using dedicated vehicles, in accordance with relevant national legislation and international agreements.

If temperature-controlled vehicles are used, the temperature monitoring equipment used during transport should be maintained and calibrated at regular intervals. Temperature mapping under representative conditions should be carried out taking into account seasonal variations. For temperature-sensitive products, qualified equipment (e.g. thermal packaging, temperature-controlled containers or temperature-controlled vehicles) should be used to ensure correct transport conditions are maintained between the manufacturer, wholesale distributor and customer.

Chapter 10 – Specific Provisions for Brokers

This was a completely new chapter and requirement in GDP introduced in the 2013 guidelines. It describes the requirements for Brokers to be registered by the local competent authority, to have a QMS in place supported by adequate documentation. Personnel working for Brokers should received adequate training on relevant sections of GDP. There is also a requirement for Brokers to follow and apply the principles of Chapter 4, Documentation with all records made available according to national legislation but at least 5 years, the same as for wholesale distributors.

Designated Responsibilities

Chapter	Topic	Senior Management	Responsible Person	Authority (EU or MS)
1	Implementation of Quality Management System	x		
1.2 and 2.2	Appointment of Responsible Person	x		
1.2 & 2.2	Ensuring that a quality system is implemented and maintained		x	
1.2	Resources	x		
1.4	Management Review	x		
2.1 & 2.2	Conditions provided for Responsible Person by the legislation			x
2.2 (i)	Ensuring that a quality management system is implemented and maintained		X	
2.2(ii)	Focusing on the management of authorised activities and the accuracy and quality of records		X	
2.2(iii)	Ensuring the initial and continuous training programme for all personnel involved in distribution activities		X	
2.2(iv)	Coordinating and performing promptly any recall operations of medicinal products		X	
2.2(v)	Ensuring that relevant customer complaints are dealt with effectively		X	

Chapter	Topic	Senior Management	Responsible Person	Authority (EU or MS)
2.2vi	Ensuring that suppliers and customers are approved		X	
2.2(vii)	Approving any subcontract activities impacting GDP		X	
2.2(viii)	Ensuring that self-inspections are performed at appropriate regular intervals following a prearranged programme and necessary corrective measures are put in place		X	
2.2(ix)	Keeping adequate records of any delegated duties		X	
2.2(x)	Deciding on final disposition of returned, rejected, recalled or falsified products		X	
2.2(xi)	Authorising the return to saleable stock of any returned medicines		X	
2.(xii)	Ensuring that any additional requirements imposed on certain products by national law are adhered to, as foreseen in Article 83 of Directive 2001/83/EC.		X	
2.2	Maintain his/her competence in GDP through regular training		x	
8.	Get copy of self-inspection reports	X	x	

Checklist: Implementation of GDP principles at wholesale distributor

Chapter 1 Quality System

- ☐ Quality manual or equivalent documentation approach established
- ☐ Organisational structure of the distributor is defined in an organizational chart. The responsibility, role and interrelationships of all personnel is clearly indicated
- ☐ A Responsible Person (RP) is appointed by the management
- ☐ The RP has a written document clearly specifying their authority and responsibility for ensuring the Quality System is implemented and maintained
- ☐ Change Control system in place for changes to critical processes
- ☐ Change Control and Quality Management encompasses the principles of Quality Risk Management
- ☐ Management responsibilities are clearly defined with the Quality System
- ☐ The Quality System Standard Operating Procedures (SOPs) ensure product is delivered to the correct recipient within agreed and satisfactory time periods
- ☐ Appropriate corrective and preventive actions (CAPA) are taken to correct deviations and prevent them
- ☐ System for Management Review in place
- ☐ Outsourced Activities (See below, Chapter 7)

Chapter 2 Personnel

- ☐ A Responsible Person is appointed
- ☐ The RP meets the requirements of national legislation
- ☐ The RP has the appropriate competence and experience required to perform their role for the size of the organisation
- ☐ The RP has knowledge of GDP
- ☐ The RP has received and is receiving on-going GDP training
- ☐ The RP has a clear written job description defining their authority to take decisions with regard to their responsibilities
- ☐ The RP has sufficient authority, resources and responsibility to fulfill their duties
- ☐ The RP can demonstrate their compliance to GDP as a minimum for
    - The Quality Management System
    - Authorised activities
    - Accuracy and quality of records (documentation)
    - The Training Programme
    - Recall Operations
    - Customer Complaints
    - Supplier Qualification

- Customer Qualification
- Approval of Sub-Contracted / Outsourced Activities impacting GDP
- Self-Inspection
- The record of delegated duties
- The final disposition of returned, rejected, recalled, falsified products
- Approval of returns to saleable stock

☐ Sufficient personnel are employed for the size and type of business

☐ Responsibilities and roles of employees working in key positions is defined in written job descriptions, including arrangements for deputy duties

☐ All personnel involved in wholesale distribution activities are trained in GDP requirements

☐ Training includes aspects of product identification and avoidance of falsified medicines entering the supply chain, as well as checking documents for accuracy and potential falsification

☐ Specific training is provided where indicated and for specific duties e.g.

- handling of hazardous products, radioactive materials as well as products presenting special risks of abuse, narcotics or psychotropic substances, or temperature sensitive products)
- processing purchase orders for narcotics and psychotropics and applying Controlled Drugs/Narcotics permits from local authorities
- Storage of products procured from / to third countries

☐ Personnel receive initial and continuing training relevant to their tasks, based on written standard operating procedures (SOPs) according to a written training programme

☐ The practical effectiveness of training is periodically assessed and documented

☐ Appropriate procedures relating to personal hygiene are established

Chapter 3 Premises and Equipment

<u>Outsourcing activities</u>

☐ A contract is in place where premises are not directly operated by the wholesale distributor and the premises are covered by a wholesale distribution authorisation

<u>Layout of premises:</u>

☐ Unauthorised access to all areas of the authorised premises is prevented

☐ Receiving and dispatch bays protect products from prevailing weather conditions e.g. roller shutter door, curtains

☐ Segregated areas are designated for the storage of any

- product suspected of falsification
- returned product
- rejected product
- product awaiting disposal
- recalled product and medicinal products not intended for the EU market

- ☐ Radioactive materials other hazardous products and products presenting special risks of fire or explosion are stored in a dedicated area(s) with appropriate safety and security measures
- ☐ There is adequate separation between the receipt and dispatch areas and storage areas
- ☐ Rest, wash and refreshment rooms for employees are adequately separated from the storage areas

Hygiene

- ☐ Procedures relating to personnel hygiene like health, hygiene and clothing are established and observed
- ☐ Storage of food, drink, smoking materials or medication for personal use in the storage areas is prohibited
- ☐ Cleaning instructions and records are in place
- ☐ Cleaning records are in use and up to date, reviewed regularly by the RP and signed by staff
- ☐ Actions highlighted during cleaning are completed and/or referred to management where required
- ☐ Premises and storage facilities are clean and free from litter and dust
- ☐ Facilities are designed and equipped so as to afford protection against the entry of insects, rodents or other animals
- ☐ A preventive pest control programme is in place

Temperature and Environment Control

- ☐ Suitable equipment and procedures are in place to ensure adequate control of the environment
- ☐ Storage areas are temperature mapped
- ☐ Temperature monitoring equipment is located according to the results of the mapping exercise
- ☐ Controls are adequate to maintain all parts of the relevant storage area within defined temperature, humidity or light parameters
- ☐ Equipment used to control or to monitor the environment, are calibrated and their correct operation and suitability is verified at defined intervals by the appropriate methodology
- ☐ Appropriate alarm systems are in place to provide alerts when there are deviations from pre-defined storage conditions
- ☐ Alarm levels are appropriately set
- ☐ Alarms are regularly tested and temperature monitoring readings are regularly reviewed

Equipment

- ☐ Planned preventive maintenance is in place for key equipment
- ☐ Calibration of equipment is traceable to a primary standard
- ☐ Adequate records of repair, maintenance and calibration activities for key equipment is made and the results are retained
- ☐ Extent of validation and qualification activities are determined by a documented risk assessment approach and are documented in a plan

- ☐ Systems are validated/qualified prior to implementation and after any significant changes or upgrades to ensure correct installation and operation
- ☐ Evidence of satisfactory validation/qualification and acceptance of a process or piece of equipment is produced and approved by appropriate personnel
- ☐ Re-qualification following repair or maintenance is considered dependant on the scope of the changes made. Such decisions are justified utilising a risk based approach.

Computer Systems

- ☐ Detailed written descriptions of the systems are available (describing the principles, objectives, security measures and scope of the system and the main features, how the computerised system is used and the way it interacts with other systems)
- ☐ Data is entered into the computerised system or amended only by persons authorised to do so
- ☐ Data is secured by physical or electronic means against willful or accidental damage
- ☐ Data is protected by backing up at regular intervals
- ☐ Back up data is stored for a period stated in national legislation but at least 5 years at a separate, secure location

Chapter 4 Documentation

- ☐ Documents are is retained for a period stated in national legislation but at least 5 years at a separate, secure location

SOPs

- ☐ SOPs are reviewed regularly and kept up-to-date
- ☐ SOPs are approved, signed and dated by appropriate authorised persons
- ☐ Version control is applied to SOPs
- ☐ Superseded SOP versions are archived
- ☐ Inadvertent use of the superseded versions is prevented
- ☐ Superseded or obsolete SOPs are removed from workstations

Records

- ☐ For any transaction in medicinal products received, supplied or brokered, records are kept either in the form of purchase/sales invoices, delivery slips, or on computer or in any other form
- ☐ Records include the following information:
    - Date
    - name of the medicinal product
    - quantity received, supplied or brokered
    - name and address of the supplier, broker or consignee, as appropriate
    - batch number where required

- ☐ Distribution records contain sufficient information on distributors and directly supplied customers (with addresses, phone and/or fax numbers inside and outside working hours, batches and quantities delivered), including those for exported products and medicinal product samples

Chapter 5 Operations

- ☐ All medicinal products distributed in the EU have a marketing authorisation granted by the EU or by a Member State
- ☐ For distributors, not being the marketing authorisation holder: the marketing authorisation holder and the competent authority in the Member State - to which the medicinal product is imported of his intention - is notified of importation
- ☐ For products being exported: a wholesale distribution authorisation or a manufacturing authorisation is in place. This is also the case if the exporting wholesale distributor is operation from a free zone.

<u>Supplier Qualification</u>

- ☐ All supplies of medicinal products are obtained only from persons/organisations who are in possession of a wholesale distribution authorisation, or who are in possession of a manufacturing authorisation which covers the product in question
- ☐ When medicinal product is obtained from another wholesale distributor: compliance with the principles and guidelines of good distribution practices of the supplying wholesale distributor is verified
- ☐ When medicinal product is obtained from manufacturer or importer: manufacturer or importer holds a manufacturing authorisation
- ☐ When medicinal product is obtained from a broker: broker is registered and complies with the requirements in Chapter 10 of the Commission Guidelines on Good Distribution Practice of Medicinal Products for Human Use
- ☐ The purchase of medicinal products is controlled by written procedures
- ☐ The supply chain of medicinal products is known and documented
- ☐ Appropriate qualification is performed prior to any procurement
- ☐ Qualification and approval of suppliers is controlled by a standard operating procedure
- ☐ The results of qualification and approval of suppliers are documented
- ☐ The results of qualification and approval of suppliers are periodically rechecked
- ☐ Qualification and approval of new suppliers: A risk based approach is used considering
    - o searches for the new supplier's reputation or reliability and its authorised activities
    - o possible target of falsification
    - o large offers of medicinal product which are generally only available in limited quantities
    - o out of range prices

<u>Qualification of Customers</u>

- ☐ Medicinal products are only supplied to persons/organisations who are themselves in possession of a distribution authorisation or who are authorized or entitled to supply medicinal products to the public
- ☐ Qualification of customers and periodic re-checks include:
  - o requesting copies of customer's authorisations
  - o verifying status on an authority website
  - o requesting evidence of qualifications or entitlement according to national legislation.
- ☐ Qualification of customers are appropriately documented

Receipt of Goods

- ☐ When receiving medicinal products from third countries for the purpose of importation: manufacturing/import authorisation is in place
- ☐ It is ensured that that the arriving consignment is correct, the medicinal products originate from approved suppliers and have not been damaged or altered during transportation
- ☐ Medicinal products which require special storage or security measures, are transferred to appropriate storage facilities immediately after appropriate checks have been conducted
- ☐ In the event of any suspicion of falsified medicinal product, the batch is immediately segregated
- ☐ In the event of any suspicion of falsified medicinal product, the batch is immediately reported to the national competent authority
- ☐ In the event of any suspicion of falsified medicinal product, the batch is immediately reported to the marketing authorisation holder (where applicable)
- ☐ Batches of medicinal products intended for the Union market are only transferred to saleable stock before assurance has been obtained that they are authorised and released for sale for the market in question
- ☐ Incoming containers of medicinal products are cleaned, if necessary, before storage

Storage

- ☐ Medicinal products are stored separately from other products
- ☐ Medicinal products are protected from harmful effects of light, temperature, moisture or other external factors.
- ☐ Particular attention is paid to products where specific storage conditions are required
- ☐ Stock rotation according to the expiry dates of batches of medicinal products is performed ("first expired first out" - FEFO - basis.)
- ☐ Medicinal products beyond their expiry date or shelf life are withdrawn immediately from saleable stock either physically or through other equivalent electronic segregation
- ☐ Physical removal of unsuitable stock is performed regularly
- ☐ Medicinal products are not stored directly on the floor
- ☐ Stock inventories are performed regularly (timings are defined using a risk based approach)
- ☐ Inventory irregularities are investigated and documented

Segregation of Goods

- ☐ Segregation is provided for the storage of rejected, expired, recalled or returned products and suspected falsified medicinal products
- ☐ Any system replacing physical segregation such as electronic segregation based on a computerised system provides equivalent security and is validated

Destruction of obsolete Goods

- ☐ Medicinal products intended to be destroyed are kept separately and handled in accordance with a written procedure
- ☐ Destruction of medicinal products is in accordance with national or international requirements for disposal of such products
- ☐ Records of all destroyed medicinal products are maintained

Picking and packing

- ☐ Controls are in place to ensure the correct product is picked
- ☐ Products have an appropriate remaining shelf life when picked
- ☐ Products are picked on a "first expired first out" (FEFO) basis
- ☐ Packing is adequate to maintain the storage conditions of the product during transport

Export (exceptions)

The rules for wholesale distribution apply in their entirety in the case of export of medicinal products, with the following exceptions:

a. The medicinal product does not have to be covered by a marketing authorisation of the EU or a Member State;

b. The customer does not have to be holder of a distribution authorisation;

c. Moreover, where the medicinal product intended for exportation has been obtained directly from another third country, without the product being prior to that placed on the market (i.e. without prior import), the supplier does not have to bear a wholesale distribution authorisation.

Chapter 6 Complaints, Returns, suspected falsified Medicinal Products and Medicinal Product Recalls

Complaints

- ☐ A written procedure is in place for the handling of complaints
- ☐ Distinction is made between complaints about the quality of a medicinal product and those relating to distribution
    - o In the case of a complaint about the quality of a medicinal product, the manufacturer and/or marketing authorisation holder is informed without delay
- ☐ A person is appointed for handling the complaints with sufficient supporting personnel
- ☐ Any complaint concerning a potential product defect or a potential falsified product is recorded

with all the original details and investigated

- ☐ The national competent authority is notified without delay in case of a potential product defect or a potential falsified product
- ☐ Any product distribution complaint is thoroughly investigated
- ☐ Appropriate follow-up actions are taken after investigation and evaluation of the complaint

Returned Medicinal Products

- ☐ Written procedures are in place for the handling and acceptance of returned medicinal products
- ☐ Medicinal products which have left the premises of the distributor are only returned to saleable stock if:
  - o the medicinal products are in their unopened and undamaged secondary packaging and in good condition
  - o medicinal products returns from a customer not holding a wholesale distribution are returned within five days, or as specified in national legislation, of original dispatch
  - o it is demonstrated that the medicinal products have been transported, stored and handled under proper specified/predefined conditions
  - o they have been examined and assessed by a sufficiently trained and competent person authorised to do so
  - o the distributor has reasonable evidence that the product was supplied to that customer
  - o the batch number of the dispatched product is known
  - o a copy of the original delivery note is attached
  - o there is no reason to believe that the product has been falsified
  - o there is evidence that the product has been stored within the authorised storage conditions throughout the entire time
- ☐ A Risk Assessment is performed taking into account
  - o the product concerned
  - o any specific storage requirements
  - o the time elapsed since the medicinal product was originally dispatched
- ☐ Returned medicinal products are kept segregated from saleable stock until a decision is taken regarding their disposition by the RP
- ☐ Returned medicinal products requiring specific temperature storage conditions such as low temperature are accompanied by documented evidence that the product has been stored under the authorised storage conditions throughout the entire time
- ☐ Products returned to saleable stock are placed that the "first expired first out" (FEFO) system operates effectively
- ☐ All handling of returned medicinal products including their return to saleable stock or disposal are approved by the Responsible Person and recorded

Suspected falsified Medicinal Products

- ☐ The staff are aware of the risks of falsified medicinal products entering the supply chain
- ☐ A procedure is in place describing immediate information of the competent authority (and, where applicable, the marketing authorisation holder of the medicinal products they identify as falsified or suspect to be falsified
- ☐ Any suspected falsified medicinal products found in the supply chain is immediately physically and securely segregated from legitimate medicinal products
- ☐ All relevant activities are recorded
- ☐ All documents and all records are retained and retrievable

Medicinal Product Recalls

- ☐ There is a written procedure for the management of recalls
- ☐ The management of recalls and its effectiveness is periodically tested and evaluated (Mock Recall)
- ☐ Any recall operation is recorded at the time it is carried out
- ☐ The distribution records are readily available to the person(s) responsible for the recall
- ☐ The records contain information on
    - Distributors and Directly Supplied Customers, with
        - Addresses
        - Phone and/or fax numbers during inside and outside of working hours
        - Email addresses
        - Batch numbers at least for products bearing safety features as required by legislation
        - Quantities
    - The records include those for
        - Exported Products
        - Medicinal Product Samples
- ☐ The progress of a recall process is recorded and a final report issued (including reconciliation between the delivered and recovered quantities of the medicinal products)

Chapter 7 Outsourced Activities

- ☐ Contracts are in place for any GDP-related activity, covering all wholesale distribution activities and clearly establish the duties and responsibilities of each party
- ☐ Contract acceptor holds a distribution authorisation as relevant where activities require a Competent Authority authorisation
- ☐ Where required, the Contract Acceptor has adequate
    - Premises
    - Equipment
    - Procedures
    - Knowledge and Experience

- Competent personnel to carry out the work ordered by the Contract Giver

☐ An audit of the Contract Acceptor is performed before the beginning of the outsourced activities

☐ A Technical Quality Agreement is established and agreed between the Contract Giver and Contract Acceptor prior to commencing the outsourced activity

☐ The Contract and Technical Quality Agreement lay out the requirement for the Contract Giver to notify the Contract Acceptor prior to further outsourcing any activities

☐ Where activities are further sub-contracted the Contract Acceptor has made appropriate arrangements with their third party to ensure the wholesale distribution information is made available in the same way as between the original Contract Giver and Contract Acceptor

☐ After the beginning of the outsourced activities audits are performed periodically

☐ Audits are performed where there is a change to the outsourced activities

☐ The Contract Giver has provided all relevant information to the Contract Acceptor to enable the contracted activities to be carried out in accordance with the specific product requirements and any other relevant requirements

Chapter 8 Self-Inspections

☐ A self-inspection programme is implemented to cover all aspects of GDP and compliance within a defined time frame

☐ Self-inspections are conducted in an independentand detailed manner (by designated competent person(s) from the company and independent external experts)

☐ Subcontracted activities are a part of the self-inspection programme

☐ Reports contain all observations

☐ A copy of the report is submitted to the organisation's management and other relevant personnel

☐ Causes of irregularities and/or deficiencies are determined and the CAPA is documented and followed-up

Chapter 9 Transportation

<u>Vehicles and equipment</u>

☐ Required storage conditions are maintained during transportation

☐ Vehicles and equipment are suitable and appropriately equipped to prevent exposure of the products to conditions that could affect their quality and packaging integrity, and to prevent contamination of any kind

☐ Procedures are in place for the operation and maintenance of all vehicles and equipment, including cleaning and safety precautions

☐ Validated temperature-control systems (e.g. thermal packaging, temperature-controlled containers, and refrigerated vehicles) are used to ensure correct transport conditions

☐ If refrigerated vehicles are used temperature mapping is performed under representative

conditions including seasonal variations

- ☐ Equipment used for temperature monitoring during transport within vehicles and/or containers, is maintained and calibrated at regular intervals at least once a year
- ☐ Risk assessment of delivery routes has been performed to ensure appropriate temperature controls are in place for
    - In-bound product
    - Out-bound product
        - E.g. review of live temperature records, dummy sample deliveries
- ☐ If cool-packs are used in insulated boxes, they are located such that the product does not come in direct contact with the cool-pack
- ☐ If cool-packs are used in insulated boxes, staff are trained on the procedures for assembly of the insulated boxes (seasonal configurations) and on the reuse of cool-packs. The process for delivery of sensitive products and control of seasonal temperature variations is described in written procedures
- ☐ Procedures cover management of unexpected occurrences such as vehicle breakdown or non-delivery
- ☐ A procedure is in place for investigating and handling temperature excursions
- ☐ Where non-dedicated vehicles and equipment are used procedures are in place to ensure that the quality of the medicinal product will not be compromised

Delivery

- ☐ Delivery drivers (including contract drivers) are trained in the relevant areas of GDP
- ☐ Deliveries are made directly to the address stated on the delivery note
- ☐ Deliveries are handed into the care of the consignee
- ☐ Deliveries are not left on alternative premises
- ☐ Procedures are in place for out of hours/unscheduled deliveries with responsibilities stated for specified persons

Transportation hubs

- ☐ When using transportation hubs, the time limit for storage in these locations is defined
- ☐ When using transportation hubs, premises are audited and approved prior to deployment
- ☐ A minimum specification for transport hubs is available
- ☐ a list of Hubs used by the transportation company is available

Deviations

- ☐ Deviations are reported to the distributor and recipient
- ☐ Where necessary in the case of deviations, the manufacturer of the medicinal product is contacted for information about appropriate steps to be taken

Containers, packaging and labeling

☐ Container and packaging is selected based on:

- the storage and transportation requirements
- the space required for the amount of medicines
- the anticipated external temperature extremes
- the estimated maximum time for transportation including transit storage at customs
- the validation status of the packaging and shipment containers

☐ The containers in which medicinal products are shipped are sealed

☐ A document is enclosed to ascertain the following:

- date
- name and pharmaceutical form of the medicinal product
- batch number at least for products bearing the safety features, where required
- quantity supplied
- name and address of the supplier
- name and delivery address of the consignee (actual physical storage premises, if different)
- applicable transport and storage conditions

☐ Containers bear labels providing sufficient information on handling and storage requirements and precautions

☐ Containers bear labels enable identification

Transportation of Products requiring special Conditions

☐ Requirements laid down by the concerned Member States are met

☐ Additional control systems in place e.g. for

- Special Containers
- Picking/Packing/Packaging of goods
- Training on procedures for assembly of insulating boxes (passive / active)
- Conditioning and re-use of cool packs with segregation of frozen and chilled ice packs

☐ Transportation is performed in safe, dedicated and secure containers and vehicles

Checklist: Implementation of GDP principles at broker

☐ The marketing authorisation holder and the competent authority in the Member State - to which the medicinal product is imported of his intention - is notified of importation

☐ The broker is registered

☐ The broker has a permanent address and contact details in the Union under which they are registered

☐ The broker notifies the competent authority of any changes thereof without unnecessary delay

- ☐ The quality system is defined in writing, approved and kept up-to date
- ☐ The quality system sets out the responsibilities, processes and risk management
- ☐ Personnel involved in brokering activities is trained in the applicable EU and national legislation and in the issues concerning falsified medicinal products
- ☐ At least the following procedures and instructions are in place:
  - Procedure for complaints handling
  - Procedure for informing competent authorities and marketing authorisation holders of suspected falsified medicinal products
  - Procedure for supporting recalls
  - Procedure for ensuring that medicinal products brokered have a marketing authorisation
  - Procedure for verifying that their supplying wholesale distributors hold a distribution authorisation, their supplying manufacturers or importers hold a manufacturing authorisation and their customers are authorised to supply medicinal products in the Member State concerned
- ☐ Records are kept for any transaction in medicinal products brokered including at least the following information:
  - date
  - name of the medicinal product
  - quantity brokered
  - name and address of the supplier and the customer
  - batch numbers of the medicinal product, where required
- ☐ Records are retained for at least 5 years or longer if required by national legislation

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