Guidelines on Good Storage and Distribution Practices of Pharmaceutical Products in Lebanon

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Edition 2

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Introduction

Distribution is an important activity in the integrated supply chain management of pharmaceutical products that involves various members responsible for the handling, storage and distribution of such products.

The objective of these guidelines is to ensure the quality and identity of pharmaceutical products during the whole distribution process. Furthermore, it sets out appropriate steps to assist in fulfilling the responsibilities involved in the different aspects of the distribution process within the supply chain and to avoid the introduction of counterfeits products into the marketplace via the distribution chain.

These guidelines are issued, according to the guidelines and instructions of the World Health Warehouse, by the Lebanese Ministry of Health, which stresses the importance of adhering to it by all parties involved in any aspect of the distribution of pharmaceutical products, as relevant to the particular role that they play, from the premises of the manufacturer of the product to the person dispensing or providing pharmaceutical products directly to a patient or his agent.

Glossary

The definitions provided below apply to the words and sentences used on these guidelines:

Active pharmaceutical ingredient (AFI)
Any substance or mixture of substances intended to be used in the manufacture of a pharmaceutical dosage form and that, when used in the production of a drug, becomes an active ingredient of that drug. Such substances are intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment or prevention of disease, or to affect the structure and function of the body. [5]

Agent
The party involved in providing, either directly or indirectly, any service related to clearing and forwarding operations, in any form, to any other party. [1] [5]

Agreement
Arrangement undertaken by and legally binding on parties. [1]

Auditing
An independent and objective activity designed to add value and improve an warehouse's operations by helping the warehouse to accomplish its objectives by using a systematic, disciplined approach to evaluate and improve the effectiveness of risk management, control and governance processes. [1]

Batch
A defined quantity of pharmaceutical products processed in a single process or series of processes so that it is expected to be homogeneous. [1] [5]

Batch number
A distinctive combination of numbers and/or letters used to uniquely identify a batch, for example, on the labels, its batch records and corresponding certificates of analysis. [1] [5]

Consignment (delivery)
The quantity of pharmaceutical(s) made by one manufacturer and supplied at one time in response to a particular request or order. A consignment may comprise one or more packages or containers and may include material belonging to more than one batch. [5]

Contamination
The undesired introduction of impurities of a chemical or microbiological nature, or of foreign matter, into or on to a starting material, intermediate or pharmaceutical product during handling, production, sampling, packaging or repackaging, storage or transportation. [1] [5]

Counterfeit pharmaceutical product
A pharmaceutical product deliberately and fraudulently mislabeled, with respect to identity and/or source. Counterfeiting can apply to both branded and generic products, and counterfeit pharmaceutical products may include products with the correct ingredients, with the wrong ingredients, without active ingredients, with an incorrect quantity of active ingredient or with fake packaging. [1] [5]

Contract
Business agreement for the supply of goods or performance of work at a specified price. [1]

Cross-contamination
The contamination of starting materials, intermediate products or finished pharmaceutical products with other starting materials or products during production, storage and transportation. [1] [5]

Distribution
The procuring, purchasing, holding, storing, selling, supplying, importing, exporting, or movement of pharmaceutical products, with the exception of the dispensing or providing pharmaceutical products directly to a patient or his or her agent. [1]

End product
Any pharmacological substance intended for human use that have exceeded all stages of the production process, including packaging containers in the final. [1]

Expiry date
The date given on the individual container (usually on the label) of a pharmaceutical product up to and including the date on which the product is expected to remain within specifications, if stored correctly. It is established for each batch by adding the shelf-life to the date of manufacture. [1] [5]

First expiry/First out (FEFO)
A distribution procedure that ensures that the stock with the earliest expiry date is distributed and/or used before an identical stock item with a later expiry date is distributed and/or used. [1]

Good Distribution Practices (GDP)
That part of quality assurance that ensures that the quality of a pharmaceutical product is maintained by means of adequate control of the numerous activities which occur during the distribution process as well as providing a tool to secure the distribution system from counterfeits, unapproved, illegally imported, stolen, counterfeit, substandard, adulterated, and/or misbranded pharmaceutical products. [1]

Good Manufacturing Practices (GMP)
That part of quality assurance which ensures that pharmaceutical products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization. [1]

Good Storage Practices (GSP)
That part of quality assurance that ensures that the quality of pharmaceutical products is maintained by means of adequate control throughout the storage thereof. [1]

Labeling
Process of identifying a pharmaceutical product including the following information, as appropriate: name of the product; active ingredient(s), type and amount; batch number; expiry date; special storage conditions or handling precautions; directions for use, warnings and precautions; names and addresses of the manufacturer and/or the supplier. [1] [5]

Manufacture
All operations of, purchase of materials and products, production, packaging, labeling, quality control, release, storage and distribution of pharmaceutical products and the related controls. [1] [5]

Material
A general term used to denote starting materials (active pharmaceutical ingredients and excipients), reagents, solvents, process aids, and intermediates, packaging materials and labeling materials. [1] [5]

Packaging Material
Any material, including printed material, employed in the packaging of a pharmaceutical product but excluding any other packaging used for transportation or shipment. Packaging materials are referred to as primary or secondary according to whether or not they are in direct contact with the product. [5]

Pharmaceutical product
Any product intended for human use, or veterinary product intended for administration to food-producing animals, presented in its finished dosage form, which is subject to control by pharmaceutical legislation in either the exporting or the importing state and includes products for which a prescription is required, products which may be sold to patients without a prescription, biologicals and vaccines. It does not, however, include medical devices. [1] [5]

Product recall
A process for withdrawing or removing a pharmaceutical product from the pharmaceutical distribution chain because of defects in the product, complaints of serious adverse reactions to the product and/or concerns that the product is or may be counterfeit. The recall might be initiated by the manufacturer, importer, wholesaler, distributor or a responsible agency. [1] [5]

Quality assurance
A wide-ranging concept covering, all matters that individually or collectively influence the quality of a product. It is the totality of the arrangements made with the object of ensuring that pharmaceutical products are of the quality required for their intended use. [1] [5]

Quality control
All measures taken including the setting of specifications, sampling, testing and analytical clearance, to ensure that sampling materials, intermediates, packaging materials and finished pharmaceutical products conform with established specifications for identity, strength, purity and other characteristics. [5]

Quality system
An appropriate infrastructure encompassing the warehouseal structure, procedures, processes and resources and systematic actions necessary to ensure adequate confidence that a product (or services) will satisfy given requirements for quality. [1] [5]

Quarantine
The status of pharmaceutical products isolated physically or by other effective means, while a decision is awaited on their release, rejection or reprocessing. [1] [5]

Retest date
The date when a material should be re-examined to ensure it is suitable for use. [5]

Shelf-life
The period of time during which a pharmaceutical product, if stored correctly, is expected to comply with the specification as determined by stability studies on a number of batches of the product. [6]

Standard operating procedure (SOP)
An authorized, written procedure giving instructions for performing operations not necessarily specific to a given product but of a more general nature (e.g. equipment operation, maintenance and cleaning, validation, cleaning of premises and environmental control, sampling and inspection). [1] [5]

Storage
The storing of pharmaceutical products and material up to the point of use from end user. [1] [5]

Supplier
A person or entity engaged in the activity of providing products and/or services upon request.

Validation
A documented program that provides a high degree of assurance that a specific process, method or system will consistently produce a result meeting pre-determined acceptance criteria. [1] [5]

Vehicles
Trucks, vans, buses, minibuses, cars, trailers, aircraft, railway carriages, boats and other means which are used to convey pharmaceutical products. [1] [5]

Storage conditions
Some pharmaceutical products require specific conditions to be stored within, and needs special instructions for storage handling and methods:

- Not to exceed 30 Degree Celsius: means to store within the range from +2 to +30 Degrees Celsius.
- Not to exceed 25 Degree Celsius: means to store within the range from +2 to +25 Degrees Celsius.
- Not to exceed 15 Degree Celsius: means to store within the range from +2 to +15 Degrees Celsius.
- Not to exceed 8 Degree Celsius: means to store within the range from +8 to +25 Degree Celsius.
- The product should be protected from humidity: means to protect it from conditions where humidity exceeds 60%, and should be kept in a humidity resistant container.
- Keep away from light: means that should be stored in places not exposed to light. It should be kept in light proof containers. [1] [5]

Quality
The degree to which a set of inherent characteristics fulfills requirements. [4]

Continuous improvement
The recurring activity to increase the ability to fulfill requirements. [4]

Corrective actions
Action to eliminate the cause of a detected nonconformity or other undesirable situation. [4]

Preventive actions
Action to eliminate the cause of a potential nonconformity or other undesirable potential situation. [4]

Correction
Action to eliminate a detected nonconformity. [4]

Plan Do Check Act

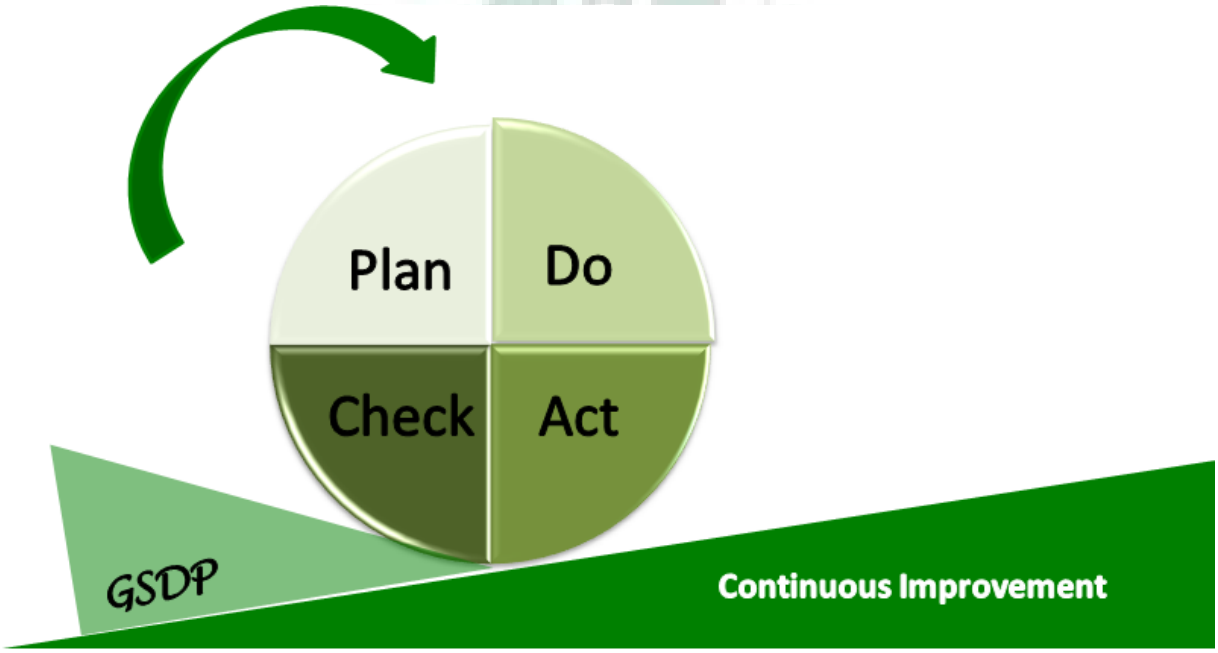
The methodology known as "Plan-Do-Check-Act" can be applied to all processes. It can be briefly described as follows:

Plan: establish the objectives and processes necessary to deliver results in accordance with customer requirements and the warehouse's policies.

Do: implement the processes.

Check: monitor and measure processes and product against policies, objectives and requirements for the product and report the results.

Act: take actions to continually improve process performance. [4]



1. Organization and management

1.1 There should be an adequate organizational structure for each entity, defined with the aid of an organizational chart that clearly identifies responsibilities, authorities and interrelationships of all personnel. [1] [6]

1.2 Duties and responsibilities should be clearly defined through documented job descriptions and understood by the concerned individuals, who should be trained on their respective duties and responsibilities and who should be aware of the relevance and importance of their activities and how they contribute to the achievement of the quality objectives. [1] [4] [6]

1.3 A designated competent person should be appointed within the warehouse, who has defined authority and responsibility for ensuring that a quality system is implemented and maintained. He shall be accountable on reporting to top management on the performance of the quality management system and any need for improvement and ensuring the promotion of awareness of customer requirements throughout the warehouse. [1] [4] [6]

1.4 There should be arrangements in place to ensure that management and personnel are not subject to commercial, political, financial and other pressures or conflict of interest that may have an adverse effect on the quality of service provided or on the integrity of pharmaceutical products. [1] [6]

1.5 The organization shall determine, provide and maintain the infrastructure needed to achieve conformity to product requirements. Infrastructure includes, as applicable,

- Buildings, workspace and associated utilities
- Process equipment (hardware and software)
- Supporting services (such as transport, communication or information systems) [4]

1.6 The organization shall determine and manage the work environment needed to achieve conformity to product requirements. The term “work environment” related to those conditions under which work is performed including physical, environment and other factors (such as noise, temperature, humidity, lighting or weather). [4]

2. Personnel

2.1 All personnel involved in the distribution activities should be competent on the basis of appropriate education, training, skills and experience in the requirements of good distribution and storage practices, as applicable. [1] [4] [6]

2.2 The warehouse should determine the necessary competency for personnel involved in the different aspects of the distribution process within the supply chain and should provide training to achieve the necessary competency. [1] [4] [6]

2.3 Personnel training should be based on written standard operating procedures (SOPs). They should receive initial and continuing training relevant to their tasks, in accordance with a written training program and they should be assessed as applicable to evaluate the effectiveness of the actions taken. Appropriate records should be maintained, including details of subjects covered and participants trained. [1] [4] [6]

2.4 Delivered trainings should cover the topic of product security, as well as aspects of product identification, the detection of counterfeits and the avoidance of counterfeits entering the supply chain. [1] [4] [6]

2.5 There should be an adequate number of competent personnel involved in all stages of the distribution of pharmaceutical products in order to ensure that the quality of the product is maintained. [1] [4] [6]

2.6 Safety procedures relating to all relevant aspects including the safety of personnel and property, environmental protection and product integrity, should be in place. [1] [6]

2.7 Personnel dealing with hazardous pharmaceutical products (such as highly active materials, radioactive materials, narcotics, and other hazardous, environmentally sensitive and/or dangerous pharmaceutical products, as well as products presenting special risks of abuse, fire or explosion) should be given specific training. [1] [6]

2.8 Personnel involved in the distribution of pharmaceutical products should wear garments suitable for the activities that they perform. Personnel dealing with hazardous pharmaceutical products, including products containing materials that are highly active, toxic, and infectious or sensitizing, should be provided with protective garments as necessary. [1] [4] [6]

2.9 Appropriate procedures relating to personnel hygiene, relevant to the activities to be carried out, should be established and observed. Such procedures should cover health, hygiene and clothing of personnel. [1] [6]

2.10 Codes of practice and punitive procedures should be in place to prevent and address situations where persons involved in the distribution of pharmaceutical products are suspected of, or found to be implicated in, any activities relating to the misappropriation, tampering, diversion or counterfeiting of any product. [1] [6]

3. Quality system & traceability of pharmaceutical products

3.1 There should be a documented quality policy describing the overall intentions and requirements of the distributor regarding quality, and including a commitment to comply with those requirements and continually improve the effectiveness of the quality system, as formally expressed and authorized by management. This policy should be communicated and understood within the warehouse. [1] [4] [6]

3.2 Inspection, auditing and certification of compliance with a quality system (such as the applicable International Standardization Warehouse (ISO) series, or national or international guidelines) by external bodies is recommended. Such certification should not, however, be seen as a substitute for compliance with these guidelines and the applicable principles of good manufacturing practices relating to pharmaceutical products. [1] [6]

3.3 Distributors should from time to time conduct risk assessments to assess potential risks to the quality and integrity of pharmaceutical products. The quality system should be developed and implemented to address any potential risks identified. The quality system should be reviewed and revised periodically to address new risks identified during the risk assessment. [1] [5]

3.4 Authorized procurement and release procedures for all administrative and technical operations performed should be in place to ensure that appropriate pharmaceutical products are sourced only from approved suppliers and distributed by approved entities. The approval should come from the competent authority of the individual country where the legal entity is registered. [1] [5]

3.5 Traceability systems should exist to enforce existing systems. Written procedures should be in place for use in situations where pharmaceutical products are suspected of being or are found to be counterfeit. [1] [6]

3.6 All parties involved in the supply chain should be identified, depending on the product's type and national policies and legislations. [1] [6]

3.7 The quality system should include provisions to ensure that the holder of the marketing authorization, entity identified on the label (if different from the manufacturer), the appropriate national and/or international regulatory bodies, as well as other relevant competent authorities, would be informed immediately in a case of confirmed or suspected counterfeiting of a pharmaceutical product. Such products should be stored in a secure, segregated area and clearly identified to prevent further distribution or sale. [1] [5]

3.8 Top management shall review the organization's quality management system at planned intervals to ensure its continuing suitability, adequacy and effectiveness. This review shall include assessing opportunities for improvement and the need for changes. [4]

3.9 Records from management review shall be maintained. The inputs to management review shall include information on results of audits, customer feedback, process performance and product conformity, status of preventive and corrective actions and follow-up actions from previous management reviews. [4]

4. Premises, warehousing and storage

Storage areas

4.1 Storage areas should be of sufficient capacity to allow the orderly storage of the various categories of pharmaceutical products, namely commercial and non-commercial products, products in quarantine, and released, rejected, returned or recalled products as well as those suspected to be counterfeits. [1] [5]

4.2 Storage areas should be designed or adapted to ensure appropriate and good storage conditions. In particular, they should be clean and dry and maintained within acceptable temperature limits. Pharmaceutical products should be stored off the floor and suitably spaced to permit cleaning and inspection. Pallets should be kept in a good state of cleanliness and repair. [1] [5]

4.3 Storage areas should be provided with adequate lighting to enable all operations to be carried out accurately and safely. [1] [5]

4.4 Warehouses in charge of distribution must ensure that premises and storage areas undergo regularly a pest control program or must ensure that pest control activities are subcontracted to a specialized entity followed up regularly. [1] [5]

4.5 Precautions must be taken to prevent unauthorized persons from entering storage areas. [1] [5]

4.6 Receiving and dispatch bays should protect pharmaceutical products from the weather. Receiving areas should be designed and equipped to allow incoming containers of pharmaceutical products to be cleaned, if necessary, before storage. [1] [5]

4.7 Physical or other equivalent validated segregation should be provided for the storage of rejected, expired, recalled or returned products and suspected counterfeits. The products and the areas concerned should be appropriately identified during their temporary storage until a decision as to their future has been made. [1] [5]

4.8 Where quarantine status is ensured by storage in separate areas, these areas must be clearly marked and access restricted to authorized personnel. Any system replacing physical quarantine should provide equivalent security. For example, computerized systems can be used, provided that they are validated to demonstrate security of access. [1] [5]

4.9 Drugs should be stored in designated areas according to the Act No. 673/98.

4.10 A system should be in place to ensure that the pharmaceutical products due to expire first are sold and/or distributed first (first expiry/ first out (FEFO)). Exceptions may be permitted as appropriate, provided that adequate controls are in place to prevent the distribution of expired products. [1] [5]

Storage conditions and stock control

4.11 Storage conditions for pharmaceutical products should be in compliance with the recommendations of the manufacturer. [1] [5]

4.12 Records of temperature and humidity monitoring data should be available for review. There should be defined intervals for checking temperature.

4.13 The equipment used for monitoring should be checked at suitable predetermined intervals and the results of such checks should be recorded and retained. All monitoring records should be kept for at least the shelf-life of the stored pharmaceutical product plus one year. Temperature mapping should show uniformity of the temperature across the storage facility. [1] [5]

4.14 Periodic stock reconciliation should be performed. Stock discrepancies should be investigated in accordance with a specified procedure to check that there have been no incorrect issues and receipts, thefts and/or misappropriations of pharmaceutical products. Documentation relating to the investigation should be kept for a predetermined period. [1] [5]

5. Vehicles and equipment

5.1 There should be procedures in place for the operation and maintenance of all vehicles and equipment involved in the distribution process, including cleaning and safety precautions. [1] [5]

5.2 Vehicles and equipment used to distribute, store or handle pharmaceutical products should be of sufficient capacity to allow orderly storage of the various categories of pharmaceutical products, suitable for their purpose and appropriately equipped to prevent exposure of the products to conditions that could affect their stability and packaging integrity, and to prevent contamination. [1] [6]

5.3 The design and use of vehicles and equipment must aim to minimize the risk of errors and permit effective cleaning and/or maintenance to avoid contamination, build-up of dust or dirt and/or any adverse effect on the quality of the pharmaceutical products being distributed. [1] [6]

5.4 Defective vehicles and equipment should not be used and should either be labeled as such or removed from service until maintained. [1] [5]

5.5 Vehicles, containers and equipment should be kept clean and dry and free from accumulated waste. [1] [6]

5.6 Vehicles, containers and equipment should be kept free from rodents, vermin, birds and other pests. There should be written programs and records for such pest control. The cleaning and fumigation agents used should not have any adverse effect on product quality. [1] [6]

5.7 Where special storage conditions (e.g. temperature and/or relative humidity), different from, or limiting, the expected environmental conditions, are required during transportation, these should be provided, checked, monitored and recorded. All monitoring records should be kept for a minimum of the shelf-life of the product distributed plus one year, or as required by national legislation. [1] [6]

5.8 Equipment used for monitoring conditions, e.g. temperature and humidity, within vehicles and containers should be calibrated at regular intervals. [1] [6]

5.9 Measures should be in place to prevent unauthorized persons from entering and/or tampering with vehicles and/or equipment, as well as to prevent the theft or misappropriation thereof. [1] [6]

5.10 Mechanisms should be available to allow for the segregation during transit of rejected, recalled and returned pharmaceutical products as well as those suspected of being counterfeits. Such goods should be securely packaged, clearly labeled, and be accompanied by appropriate supporting documentation. [1] [6]

5.11 Where feasible, consideration should be given to adding technology, such as global positioning system (GPS) electronic tracking devices and others, which would enhance the security of pharmaceutical products while in the vehicle. [1]

5.12 Where third-party carriers are used, distributors should develop written agreements with carriers to ensure that appropriate measures are taken to safeguard pharmaceutical products, including maintaining appropriate documentation and records. [1] [6]

6. Shipment containers and container labeling

6.1 Pharmaceutical products should be stored and distributed in shipment containers that have no adverse effect on the quality of the products, and that offer adequate protection from external influences, including contamination. [1] [6]

6.2 Shipping containers should bear labels providing sufficient information on handling and storage conditions and precautions to ensure that the products are properly handled and secure at all times. The shipment container should enable identification of the container's contents and source. [1] [6]

6.3 The need for any special transport and/or storage conditions should be stated on the shipment container label. If a pharmaceutical product is intended for transfer to areas outside the control of the manufacturer's products management system, the name and address of the manufacturer, special transport conditions and any special legal requirements, including safety symbols, should also be included on the container label. [1] [6]

6.4 Normally, internationally and/or nationally accepted abbreviations, names or codes should be used in the labeling of shipment containers. [1] [6]

6.5 Special care should be taken when using dry ice in shipment containers. In addition to safety issues it must be ensured that the pharmaceutical product does not come into contact with the dry ice, as it may have an adverse effect on the quality of the product. [1] [6]

6.6 Written procedures should be available for the handling of damaged and/or broken shipment containers. Particular attention should be paid to those containing potentially toxic and hazardous products. [1] [6]

7. Dispatch and receipt

7.1 Pharmaceutical products should only be sold and/or distributed to persons or entities that are authorized to acquire such products in accordance with the applicable national, regional and international legislation. Written proof of such authority must be obtained prior to the distribution of products to such persons or entities. [1] [5]

7.2 The dispatch and transportation of pharmaceutical products should be undertaken only after the receipt of a valid delivery order. [1] [5]

7.3 Written procedures for the dispatch of pharmaceutical products should be established. Such procedures should take into account the nature of the product as well as any special precautions to be observed. Pharmaceutical products under quarantine will require release for dispatch by the person responsible for quality. [1] [5]

7.4 Records for the dispatch of pharmaceutical products should be prepared and should include at least the following information: date of dispatch; complete business name and status of the addressee (e.g. retail pharmacy, hospital or community clinic); a description of the products including, e.g. name, dosage form and strength (if applicable); quantity of the products; applicable transport and storage conditions; a unique number to allow identification of the delivery order; assigned batch number and expiry date to facilitate traceability. [1] [5]

7.5 Records of dispatch should contain enough information to enable traceability of the pharmaceutical product. Such records should facilitate the recall of a batch of a product when necessary. [1] [5]

7.6 In addition, the assigned batch number and expiry date of pharmaceutical products should be recorded at the point of receipt to facilitate traceability. [1] [5]

7.7 Methods of transportation, including vehicles to be used, should be selected with care, and local conditions should be considered, including the climate and any seasonal variations experienced. Delivery of products requiring controlled temperatures should be in accordance with the applicable storage and transport conditions. [1] [5]

7.8 Delivery schedules should be established and routes planned, taking local needs and conditions into account. Such schedules and plans should be realistic and systematic. Security risks should also be taken into account when planning the schedules and routes of the delivery. **[1] [5]**

7.9 Vehicles and containers should be loaded carefully and systematically, where applicable on a first-out/last-in basis, to save time when unloading, prevent physical damage and reduce security risks. Extra care should be taken during loading and unloading of cartons to avoid damage. **[1] [5]**

7.10 Pharmaceutical products should not be supplied or received after their expiry date, or so close to the expiry date that this date is likely to be reached before the products are used by the consumer. **[1] [5]**

7.11 Incoming shipments should be examined to verify the integrity of the container/closure system, ensure that tamper-evident packaging features are intact, and that labeling appears intact. **[1] [5]**

8. Transportation and products in transit

8.1 Products and shipment containers should be secured to prevent or provide evidence of unauthorized access. Vehicles and operators should be provided with additional security, as appropriate, to prevent theft and other misappropriation of products during transportation. [1]

8.2 The people responsible for the transportation of pharmaceutical products should be informed about all relevant conditions for storage and transportation. These requirements should be adhered to throughout transportation and at any intermediate storage stages. [1] [5]

8.3 Product shipments should include the appropriate documentation to facilitate identification and verification of compliance with regulatory requirements. Policies and procedures should be followed by all persons involved in the transportation, to secure pharmaceutical products. [1] [5]

8.4 Pharmaceutical products should be stored and transported in accordance with procedures such that: • the identity of the product is not lost. • The product does not contaminate and is not contaminated by other products. • Adequate precautions are taken against spillage, breakage, misappropriation and theft. • Appropriate environmental conditions are maintained, e.g. using cold chain for thermo labile products. [1] [5]

8.5 Written procedures should be in place for investigating and dealing with any failure to comply with storage requirements, e.g. temperature deviations. [1]

8.6 The required storage conditions for pharmaceutical products should be maintained within acceptable limits during transportation. If a deviation has been noticed during transportation by the responsible for transportation, this should be reported to the distributor and recipient. In cases where the recipient notices the deviation, it should be reported to the distributor. Where necessary, the manufacturer of the pharmaceutical product should be contacted for information about appropriate steps to be taken. [1]

8.7 Where special conditions are required during transportation that are different from or limit the given environmental conditions (e.g. temperature and humidity) these should be provided by the manufacturer on the labels, monitored and recorded. [1] [5]

8.8 Transportation and storage of pharmaceutical products containing hazardous substances, such as toxic, radioactive material, and other dangerous pharmaceutical products presenting special risks of abuse, fire or explosion should be stored in safe, dedicated and secure areas, and transported in safe, suitably designed, secured containers and vehicles. [1] [5]

8.9 Products containing narcotics and other dependence-producing substances should be transported in safe and secure containers and vehicles and be stored in safe and secure areas. **[1]**

8.10 Spillages should be cleaned up as soon as possible to prevent possible contamination, cross-contamination and hazards. Written procedures should be in place for the handling of such occurrences. **[1] [6]**

8.11 Physical or other equivalent (e.g. electronic) segregation should be provided for the storage and distribution during transit of rejected, expired, recalled or returned pharmaceutical products and suspected counterfeits. The products should be appropriately identified, securely packaged, clearly labeled and be accompanied by appropriate supporting documentation. **[1]**

8.12 The interiors of vehicles and containers should remain clean and dry while pharmaceutical products are in transit. **[1] [5]**

8.13 Drivers of vehicles should identify themselves and present appropriate documentation to demonstrate that they are authorized to transport the load. **[1]**

8.14 Damage to containers and any other event or problem that occurs during transit must be recorded and reported to the relevant department, entity or authority, and investigated. **[1] [5]**

9. Documentation

9.1 Written instructions and records which document all activities relating to the storage and distribution of pharmaceutical products, including all applicable receipts and issues (invoices) should be available. Records should be kept in accordance with national regualtions. [1]

9.2 Procedures should be established and maintained for the preparation, review, approval, use of and control of changes to all documents relating to the distribution process. Procedures must be in place for both internally generated documents and those from external sources. [1]

9.3 The title, nature and purpose of each document should be clearly stated. The contents of documents should be clear and unambiguous. Documents should be laid out in an orderly fashion and be easy to check. [1]

9.4 All documents should be completed, approved, signed (as required) and dated by an appropriate authorized person(s) and should not be changed without the necessary authorization. [1]

9.5 The nature, content and retention of documentation relating to the storage and distribution of pharmaceutical products and any investigations conducted and action taken, should comply with national legislative requirements. Where such requirements are not in place, the documents should be retained for at least one year after the expiry date of the product concerned. [1]

9.6 Distributors should keep records of all pharmaceutical products received. Records should contain at least the following information: date, name of the pharmaceutical product, quantity received or supplied and name and address of the supplier. [1]

9.7 All records must be readily retrievable, and be stored and retained using facilities that are safeguarded against unauthorized modification, damage, deterioration and/or loss of documentation. [1]

9.8 Mechanisms should exist to allow for transfer of information, including quality or regulatory information, between a manufacturer and a customer, as well as the transfer of information to the relevant regulatory authority as required. [1]

9.9 Permanent records, written or electronic, should exist for each stored product indicating recommended storage conditions, any precautions to be observed and retest dates. Pharmacopoeial requirements and current national regulations concerning labels and containers should be respected at all times. [1]

9.10 Where the records are generated, there should be copies (soft and hard) kept to prevent any accidental data loss. [1]

10. Repackaging and relabeling

10.1 Repackaging and relabeling of pharmaceutical products should not be allowed, as these practices may represent a risk to the safety and security of the supply chain. [6]

10.2 Printing and/or adding extra stickers should not be allowed unless authorized by the concerned entity. [6]

10.3 The re-printing is forbidden in the law No. 367/1994 related to pharmacy profession.

11. Complaints

11.1 There should be a written procedure in place for the handling of complaints. A distinction should be made between complaints about a product or its packaging and those relating to distribution. In the case of a complaint about the quality of a product or its packaging, the original manufacturer and/ or marketing authorization holder should be informed as soon as possible. [1] [6]

11.2 All complaints and other information concerning potentially defective and potentially counterfeit pharmaceutical products should be reviewed carefully according to written procedures describing the action to be taken, including the need to consider a recall where appropriate. Consideration should be given to whether other batches of the product should also be checked. [1] [6]

11.3 Appropriate follow-up action should be taken after investigation and evaluation of the complaint. There should be a system in place to ensure that the complaint, the response received from the original product manufacturer, or the results of the investigation of the complaint, are shared with all the relevant parties. [1]

12. Recalls

12.1 There should be a system, which includes a written procedure, to effectively and promptly recall pharmaceutical products known or suspected to be defective or counterfeit, with a designated person(s) responsible for recalls. This procedure should be checked regularly and updated as necessary. [1] [6]

12.2 The original manufacturer and/or marketing authorization holder should be informed in the event of a recall. Where a recall is instituted by an entity other than the original manufacturer and/or marketing authorization holder, consultation with the original manufacturer and/or marketing authorization holder should, where possible, take place before the recall is instituted. Information on a recall should be shared with the appropriate national regulatory authority. If a recall of the original product is necessary because of a counterfeited product which is not easily distinguishable from the original product, the manufacturer of the original product and the relevant health authority should be informed. [1] [6]

12.3 The effectiveness of the arrangements for recalls should be evaluated at regular intervals. [1] [6]

12.4 Recalled pharmaceutical products should be segregated during transit and clearly labeled as recalled products. All recalled pharmaceutical products should be stored in a secure, segregated area pending appropriate action. [1] [6]

12.5 The particular storage conditions applicable to a pharmaceutical product which is subject to recall should be maintained during storage and transit until such time as a decision has been made regarding the fate of the product in question. [1] [6]

12.6 All customers and competent authorities of all countries to which a given pharmaceutical product may have been distributed should be informed promptly of any intention to recall the product. [1] [6]

12.7 All records should be readily available to the designated person(s) responsible for recalls. These records should contain sufficient information on pharmaceutical products supplied to customers (including exported products). [1] [6]

12.8 The progress of a recall process should be recorded and a final report issued, which includes reconciliation between delivered and recovered quantities of products. [1] [6]

13. Returned products

13.1 A distributor should receive pharmaceutical product returns or exchanges pursuant to the terms and conditions of the agreement between the distributor and the recipient. Both distributors and recipients should be accountable for administering their returns process and ensuring that the aspects of this operation are secured and do not permit the entry of counterfeit products and that provision are made for the appropriate and safe transport of returned and rejected pharmaceutical products prior to their disposal. **[1]**

13.2 The necessary assessment and decision regarding the disposition of such products must be made by a suitably authorized person. The nature of the product returned to the distributor, any special storage conditions required, its condition and history and the time elapsed since it was issued, should all be taken into account in this assessment. Where any doubt arises over the quality of a pharmaceutical product, it should not be considered suitable for reissue or reuse. **[1]**

13.3 Rejected pharmaceutical products and those returned to a distributor should be appropriately identified and handled in accordance with a procedure which involves at least: the physical segregation of such pharmaceutical products in quarantine in a dedicated area, or other equivalent (e.g. electronic segregation). **[1]**

This is to avoid confusion and prevent distribution until a decision has been taken with regard to their disposition. The particular storage conditions applicable to a pharmaceutical product which is rejected or returned should be maintained during storage and transit until such time as a decision has been made regarding the product in question. **[1]**

13.4 Pharmaceutical products that should be disposed should be manipulated in accordance with international, national and local requirements regarding disposal of such products, and with due consideration to protection of the environment. **[1]**

13.5 Records of all returned, rejected and/or destroyed pharmaceutical products should be kept for a predetermined period. **[1]**

14. Counterfeit pharmaceutical products

14.1 Counterfeit pharmaceutical products found in the distribution chain should be kept apart from other pharmaceutical products to avoid any confusion. They should be clearly labeled as not for sale and national regulatory authorities and the holder of the marketing authorization for the original product should be informed immediately. [1] [5]

14.2 The sale and distribution of a suspected counterfeit pharmaceutical product should be suspended and the national regulatory authority notified without delay. [1] [5]

14.3 Upon confirmation of the product being counterfeit a formal decision should be taken on its disposal, ensuring that it does not re-enter the market, and the decision recorded. [1] [5]

15. Importation

15.1 The number of ports of entry in a country for the handling of imports of pharmaceutical products should be limited by appropriate legislation. Such ports could be designated by the state. [1] [6]

15.2 At the port of entry, consignments of pharmaceutical products should be stored under suitable conditions for as short a time as possible. [1] [6]

15.3 All reasonable steps should be taken by importers to ensure that products are not mishandled or exposed to adverse storage conditions at wharves or airports or land fronts. [1] [6]

16. Contract activities

16.1 Any activity relating to the distribution of a pharmaceutical product which is delegated to another person or entity should be performed by parties appropriately authorized for that function and in accordance with the terms of a written contract. [1] [6]

16.2 The contract should define the responsibilities of each party including observance of the principles of good distribution practices. It should also include responsibilities of the contractor for measures to provide adequate training for involved personnel avoid the entry of counterfeit medicines into the distribution chain. [1] [6]

16.3 All contract accepters should comply with the requirements in these guidelines and should be audited periodically. [1]

17. Self-inspection

17.1 The warehouse should conduct self-inspections at planned intervals to determine whether the quality system conforms to planned arrangements, to the requirements of the GSDP guidelines and to the quality management system requirements established by the warehouse. Self-inspections allow also ensuring the quality system is effectively implemented and maintained. [1] [4] [6]

17.2 Self-inspections should be planned taking into consideration the status and importance of the processes and areas to be inspected, as well as the results of previous inspections. [1] [4] [6]

17.3 The self-inspection criteria, scope, frequency and methods should be determined. [1] [4] [6]

17.4 The selection of inspectors and conduct of inspections should ensure objectivity and impartiality of the inspection process. [1] [4] [6]

17.5 A documented procedure should be established to define the responsibilities and requirements for planning and conducting inspections, establishing records and reporting results. [1] [4] [6]

17.6 The results of all self-inspections should be recorded. Reports should contain all observations made during the inspection and, where applicable, proposals for corrective measures. There should be an effective follow-up program. Management should evaluate the inspection report and the records of any corrective actions taken. [1] [4] [6]

18. Measurement, analysis and improvement

18.1 As one of the measurements of the performance of the quality management system, the warehouse should monitor information relating to customer perception as to whether the customer requirements are met. The methods for obtaining and using this information shall be determined. [4]

18.2 The warehouse should apply suitable methods for monitoring and where applicable, measurement of the quality management system processes. These methods should demonstrate the ability of the processes to achieve planned results. When planned results are not achieved, correction and corrective action shall be taken, as appropriate. [4]

18.3 The warehouse should continuously improve the effectiveness of the quality management system through the use of the quality policy, quality objectives, audit results, analysis of data, corrective and preventive actions and management review. [4]

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