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Draft document for comments

World Health Organization

GOOD STORAGE AND DISTRIBUTION PRACTICES

(May 2019)

DRAFT FOR COMMENTS

Please send any comments you may have to Dr Sabine Kopp, Group Lead, Medicines Quality Assurance, Technologies Standards and Norms (kopps@who.int), with a copy to Ms Claire Vogel (vogelc@who.int) by 15 June 2019 .

Medicines Quality Assurance working documents will be sent out electronically only. They will also be placed on the Medicines website for comment under " Current projects ". If you have not already received our draft working documents, please send your email address (to jonessi@who.int) and we will add you to our electronic mailing list.

39 SCHEDULE FOR DRAFT WORKING DOCUMENT QAS/19.793:

40 GOOD STORAGE AND DISTRIBUTION PRACTICES

41

Description of Activity	Date
During the Fifty-third WHO Expert Committee on Specifications for Pharmaceutical Preparations (ECSPP), the Expert Committee recommended consolidation of the Good storage practices and Good distribution practices for pharmaceutical products and the elements of good distribution channel guidance into one document.	22-26 October 2018
Preparation of first draft working document by Dr Andr Zyl, a member of the Fifty-third ECSPP.	December 2018 - March 2019
Mailing of working document to the Expert Advisory Panel on the International Pharmacopoeia and Pharmaceutical Preparations (EAP) inviting comments and posting of the working document on the WHO website for public consultation.	April – June 2019
Consolidation of comments received and review of feedbacks. Preparation of working document for discussion.	June 2019
Discussion of working document and feedbacks received during the informal Consultation on Good Practices for Health Products Manufacture and Inspection.	July 2019
Revision of the working document based on comments received during the informal Consultation on Good Practices for Health Products Manufacture and Inspection.	End of July 2019
Mailing of revised working document to the EAP inviting comments and posting the working document on the WHO website for public consultation.	August – September 2019
Consolidation of comments received and review of feedbacks. Preparation of working document for discussion.	End of September 2019
Presentation to the Fifty-fourth meeting of the ECSPP.	14 -18 October 2019
Any other follow-up action as required.	

GOOD STORAGE AND DISTRIBUTION PRACTICES

1. INTRODUCTION

1.1. Storage and distribution are important activities in the supply chain management of medical products. Various people and entities are generally responsible for handling, storage and distribution. Products may be subjected to various risks at different stages in the supply chain, i.e. during purchasing, storage, distribution, transportation, repackaging, and relabelling. Further, substandard and falsified products are a real threat to public health and safety. Consequently, it is essential to protect the supply chain against the penetration of such products.

1.2. This document sets out appropriate steps to assist in ful?lling the responsibilities involved in the different stages within the supply chain and to avoid the introduction of substandard and falsified products into the market. The relevant sections should be considered as particular roles that entities play in the storage and distribution of medical products.

1.3. This guideline is intended to be applicable to all persons and outlets involved in any aspectof the storage and distribution of medical products from the premises of the manufacturer of the product to the person dispensing or providing pharmaceutical products directly to a patient or his or her agent. This includes all parties involved in trade, storage and distribution of medical products, manufacturers and wholesalers, as well as other parties such as brokers, suppliers, distributors, logistics providers, traders, transport companies and forwarding agents and their employees.

1.4. The relevant sections of this guideline should also be considered for implementation by, amongst others, governments, regulatory bodies, international procurement organizations, donor agencies and certifying bodies, as well as all parties involved in any aspect of the trade and distribution of pharmaceutical products, including health care workers.

1.5. The guidelines can also be used as a tool in the prevention of the distribution of substandard and falsified products. It should, however, be noted that these are general

guidelines which may be adapted to suit the prevailing situations and conditions in individual countries. National or regional guidelines may be developed to meet speci?c needs and situations in a particular region or country.

1.6. To maintain the original quality of medical products, every party active in the supply chain has to comply with the applicable legislation and regulations. Every activity in the storage and distribution of medical products should be carried out according to the principles of good manufacturing practices (GMP), good storage practice (GSP) and good distribution practice (GDP) as applicable.

1.7. This guideline does not deal with dispensing to patients as this is addressed in the World Health Organization (WHO) good pharmacy practice (GPP) guide (xx). These guidelines should also be read in conjunction with other WHO guidelines (xx).

2. SCOPE

2.1. This document lays down guidelines for the storage and distribution of medical products. It is closely linked to other existing guidelines recommended by the WHO Expert Committee on Specifications for Pharmaceutical Preparations, such as referenced in section (xyz).

2.2. Depending on the national and regional legislation, these guidelines may apply equally to products for human and for veterinary use. The guidelines thus cover products for which a prescription is required by the patient, products which may be provided to a patient without a prescription, biologicals, vaccines and medical devices.

2.3. The document does not speci?cally cover GMP aspects of ?nished products in bulk, distribution of labels or packaging as these aspects are considered to be covered by other guidelines. The principles for the distribution of starting materials (active pharmaceutical ingredients (APIs) and excipients) are also not covered here. These are laid down in the WHO guidance "Good Trade and Distribution Practices for Pharmaceutical Starting Materials" (7).

3. GLOSSARY

The definitions provided below apply to the words and phrases used in this guideline. Although an effort has been made to use standard definitions as far as possible, they may have different meanings in other contexts and documents

active pharmaceutical ingredient (API)

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.

ALCOA

A commonly used acronym for "attributable, legible, contemporaneous, original and accurate".

Auditing

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

batch

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

batch number

A distinctive combination of numbers and/or letters which uniquely identifies a batch, for example, on the labels, its batch records and corresponding certificates of analysis.

consignment

The quantity of pharmaceutical products supplied at one time in response to a particular request or order. A consignment may comprise of one or more packages or containers and may include pharmaceutical products belonging to more than one batch.

container

The material employed in the packaging of a pharmaceutical product. Containers include primary, secondary and transportation containers. Containers are referred to as primary if they are intended to be in direct contact with the product. Secondary containers are not intended to be in direct contact with the product.

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.

contract

Business agreement for the supply of goods or performance of work at a speci?ed price.

corrective and preventative actions (CAPA)

A system for implementing corrective actions and preventive actions resulting from an investigation of complaints, product rejections, non-conformances, recalls, deviations, audits, regulatory inspections and findings, and trends from process performance and product quality monitoring.

cross-contamination

Contamination of a starting material, intermediate product or ?nished pharmaceutical product with another starting material or product during production, storage and transportation.

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.

excipient

A substance, other than the active ingredient, which has been appropriately evaluated for safety and is included in a drug delivery system to aid in the processing of the drug delivery system during its manufacture; protect, support or enhance stability, bioavailability, or patient acceptability; assist in product identification; or enhance any other attribute of the overall safety and effectiveness of the drug during storage or use.

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.

?rst expiry/?rst 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.

forwarding agent

A person or entity engaged in providing, either directly or indirectly, any service concerned with clearing and forwarding operations in any manner to any other person and includes a consignment agent.

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.

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.

good pharmacy practice (GPP)

The practice of pharmacy aimed at providing and promoting the best use of medicines and other health care services and products, by patients and members of the public. It requires that the welfare of the patient is the pharmacist's prime concern at all times.

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.

good trade and distribution practices (GTDP)

That part of quality assurance that ensures that the quality of pharmaceutical products is maintained by means of adequate control throughout the numerous activities which occur during the trade and the distribution process.

heating, ventilation and air conditioning systems (HVAC)

Heating, ventilation and air-conditioning, also referred to as environmental control system (ECS).

importation

The act of bringing or causing any goods to be brought into a customs territory (national territory, excluding any free zone).

intermediate product

Partly processed product that must undergo further manufacturing steps before it becomes a bulk ?nished product.

labelling

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.

manufacture

All operations of purchase of materials and products, production, packaging, labelling, quality control, release, storage and distribution of pharmaceutical products, and the related controls.

marketing authorization

A legal document issued by the competent medicines regulatory authority for the purpose of marketing or free distribution of a product after evaluation for safety, ef?cacy and quality. It must set out, inter alia, the name of the product, the pharmaceutical dosage form, the quantitative formula (including excipients) per unit dose (using International Nonproprietary Names (INNs) or national generic names where they exist), the shelf life and storage conditions, and packaging characteristics. It speci?es the information on which authorization is based (e.g. " The product(s) must conform to all the details provided in your application and as modi?ed in subsequent correspondence It "a)so contains the product information approved for health professionals and the public, the sales category, the name and address of the holder of the authorization and the period of validity of the authorization. Once a product has been given marketing authorization, it is included on a list of authorized products - the register - and is often said to be " registered " or to " have registration ". Market authorization may occasionally also be referred to as a " licence " or " product licence " .

material

A general term used to denote starting materials (active pharmaceutical ingredients and excipients), reagents, solvents, process aids, intermediates, packaging materials and labelling materials.

packaging material

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

pedigree

A complete record that traces the ownership of and transactions relating to apharmaceutical product as it is distributed through the supply chain.

pharmaceutical product

Any product intended for human use, or veterinary product intended for administration to food-producing animals, presented in its ?nished 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.

product recall

A process for withdrawing or removing a pharmaceutical product from the pharmaceutical distribution chain because of defects in the product, complaintsof 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.

production

All operations involved in the preparation of a pharmaceutical product, from receipt of materials through processing, packaging and repackaging, labelling and relabelling, to completion of the finished product.

quality assurance

A wide-ranging concept covering all matters that individually or collectively in?uence 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.

quality risk management

A systematic process for the assessment, control, communication and review of risks to the quality of pharmaceutical products across the product life-cycle.

quality system

An appropriate infrastructure, encompassing the organizational structure, procedures, processes and resources and systematic actions necessary to ensure adequate con?dence that a product (or services) will satisfy given requirements for quality.

quarantine

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

retest date

The date when a material should be re-examined to ensure that it is still suitable for use.

sampling

Operations designed to obtain a representative portion of a pharmaceutical product, based on an appropriate statistical procedure, for a de?ned purpose, e.g. acceptance of consignments or batch release.

shelf life

The period of time during which a pharmaceutical product, if stored correctly, is expected to comply with the speci?cation as determined by stability studies on a number of batches of the product. The shelf life is used to establish the expiry date of each batch.

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).

storage

The storing of pharmaceutical products up to the point of use.

supplier

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

transit

The period during which pharmaceutical products are in the process of being carried, conveyed, or transported across, over or through a passage or route to reach the destination.

vehicles

Trucks, vans, buses, minibuses, cars, trailers, aircraft, railway carriages, boats and other means which are used to convey pharmaceutical products

4. GENERAL PRINCIPLES

4.1. There should be collaboration between all parties, including governments, customs agencies, law enforcement agencies, regulatory authorities, manufacturers, distributors and entities responsible for the supply of medical products to patients, to ensure the quality and safety of these products; to prevent the exposure of patients to substandard and falsified products and to ensure that the integrity of the distribution chain is maintained.

4.2. The principles of GSP and GDP should be included in national legislation and guidelines for the storage and distribution of medical products, in a country or region as applicable, as a means of establishing minimum standards. The principles of GSP and GDP are applicable to:

? products moving forward in the distribution chain from the manufacturer;

? products which are moving backwards in the chain, for example, as a result of the return or recall thereof; and

? donations of products.

5. QUALITY MANAGEMENT

Quality Systems

5.1. Entities involved in the storage and distribution of medical products must have a comprehensively designed and correctly implemented, documented, quality system that incorporates good storage practices, good distribution practices, quality risk management and management review.

5.2. Senior management has the ultimate responsibility to ensure an effective quality system is established, is adequately resourced, implemented and maintained. The effectiveness, roles, responsibilities and authorities should be defined, communicated and implemented throughout the organization.

5.3. The quality system should ensure that:

? GSP and GDP is adopted and managed through satisfactory arrangements to ensure, as far as possible, that the medical products are stored, distributed and subsequently handled so that quality is maintained throughout their shelf-life in the supply-chain;

? products are appropriately procured, stored, distributed and delivered to the right recipients;

? operations are clearly specified in a written procedures;

? responsibilities are clearly specified in job descriptions;

? all risks are identified and necessary, effective controls are implemented;

? processes are in place to assure the management of outsourced activities;

? there is a procedure for self-inspection and/or quality audit;

? there is a system for quality risk management (QRM);

? there are systems for managing returns, complaints and recalls;

? systems are in place to manage changes, deviations and corrective and preventive actions (CAPAs).

5.4. There should be an authorized, written quality policy describing the overall intentions and requirements regarding quality. This may be reflected in a quality manual.

5.5. There should be an appropriate organizational structure. This should be presented in an authorized organizational chart. The responsibility, authority and interrelationships of all personnel should be clearly indicated.

5.6. Duties and responsibilities should be clearly de?ned and understood by the individuals concerned and recorded as written job descriptions.

5.7. The quality system should include appropriate procedures, processes and resources.

6. QUALITY RISK MANAGEMENT

6.1. There should be a system to assess, control, communicate and review risks identified at all stages in the supply chain. The evaluation of the risk should be based on scientific knowledge and experience with the process and ultimately linked to the protection of the patient.

6.2. Appropriate controls should be developed and implemented to address any risks identi?ed. The effectiveness of the controls implemented should be evaluated at periodic intervals.

(For further reading, see also WHO Guideline on Risk Management and ICH Q9, ISO 31000).

7. MANAGEMENT REVIEW

7.1. There should be a system for periodic management review. The review should include:

? senior management;

- review of the quality system and its effectiveness by using quality metrics and key performance indicators;
- identification of opportunities for continual improvement; and
- follow-up on recommendations from previous management review meetings.

7.2. Records should be maintained.

8. COMPLAINTS

8.1. There should be a written procedure 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.

8.2. All complaints should be recorded and appropriately investigated. The root cause should be identified and the impact (e.g. on other batches or products) and risk assessed. Appropriate CAPA should be taken.

8.3. Where required, the national regulatory authority should be informed and a recall initiated where appropriate.

8.4. The relevant information, such as the results of the investigation of the complaint, should be shared with the relevant parties.

8.5. Product quality problems or suspected cases of substandard or falsified products are identified and these should be handled according to the relevant procedures. The information should be shared with the appropriate national and/or regional regulatory authorities.

9. RETURNED GOODS

9.1. Returned medical products should be handled in accordance with authorized procedures.

9.2. All returned goods should be placed in quarantine upon receiving. The status of the goods should be clear. Precautions should be taken to prevent access and distribution until a decision has been taken with regard to their disposition. The particular storage conditions applicable to the products should be maintained.

9.3. When handling returned goods, at least the following considerations should be taken:

? A risk-based process should be followed when deciding on the fate of the returned goods. This should include, but not be limited to, the nature of the product, storage conditions, condition of the product history, time-lapse since distribution, manner and condition of transport while being returned;

? the terms and conditions of the agreement between the parties; and

? examination of the returned goods, with decisions taken by suitably qualified, experienced and authorized persons.

9.4. Where products are rejected, authorized procedures should be followed, including safe transport.

9.5. Destruction of products should be done in accordance with international, national and local requirements regarding disposal of such products and with due consideration to the protection of the environment.

9.6. Records of all returned, rejected and destroyed medical products should be kept for a defined period.

10. RECALLS

10.1. There should be a written procedure to effectively and promptly recall medical products in compliance with national or regional requirements. A designated person(s) should be responsible for recalls.

10.2. The effectiveness of the procedure should be checked annually and updated as necessary.

10.3. The original manufacturer and/or marketing authorization holder, or other relevant contract party, should be informed in the event of a recall.

10.4. Information on a recall should be shared with the appropriate national or regional regulatory authority.

10.5. All recalled products should be transported and stored in secure, segregated conditions and clearly labelled as recalled products. The particular storage conditions applicable to the product should be maintained.

10.6. All customers and competent authorities of all countries to which a given product may have been distributed should be informed promptly of the recall of the product.

10.7. All records, including distribution records, should be readily accessible to the designated person(s) responsible for recalls. These records should contain suf?cient information on products supplied to customers (e.g. name, address, contact detail, batch numbers, quantities, safety features - including exported products).

10.8. The progress of a recall process should be recorded and a ?nal report issued which includes a reconciliation between delivered and recovered quantities of products.

11. SELF-INSPECTION

11.1. The quality system should include self-inspections. These should be conducted to monitor implementation and compliance with the principles of regulations, GSP, GDP and other appropriate guidelines.

11.2. Self-inspections should be conducted periodically according to an annual schedule.

11.3. The team conducting the inspection should be free from bias and individual members should have appropriate knowledge and experience. Audits by independent third parties may be beneficial.

11.4. The results of all self-inspections should be recorded. Reports should contain all observations made during the inspection and presented to the relevant personnel as well as management.

11.5. Necessary CAPAs should be taken and the effectiveness of the CAPAs should be reviewed.

12. PREMISES

General

12.1. Premises should be suitably located, designed, constructed and maintained to ensure appropriate operations such as receiving, storage, picking, packing and dispatch of medical products.

12.2. There should be sufficient space, lighting and ventilation to ensure required segregation, appropriate storage conditions and cleanliness.

12.3. Sufficient security should be provided and access should be controlled.

12.4. Appropriate controls and segregation should be provided for products requiring specific handling or storage such as radio-active materials, products containing hazardous substances, and products to be stored under controlled temperature and relative humidity conditions.

12.5. Receiving and dispatch bays should be separate and should protect products from weather conditions.

12.6. Activities relating to receiving and dispatch such be done in accordance with authorized procedures. Areas should be suitably equipped for the operations.

12.7. Premises should be kept clean. Cleaning equipment and cleaning agents should not become possible sources of contamination.

12.8. Premises should be protected from the entry of birds, rodents, insects and other animals. A rodent and pest control programme should be in place.

12.9. Toilets, wash, rest and canteen facilities should be separate from other areas. Food, eating, drinking, and smoking should be prohibited in all areas where medical products are stored or handled.

Receiving

12.10. Each incoming delivery should be checked against the relevant documentation to ensure that the correct product is delivered from the correct supplier. This may include, e.g. the purchase order, each container, label description, batch number, product and quantity.

12.11. The consignment should be examined for uniformity of the containers and, if necessary, should be subdivided according to the supplier's batch number should the delivery comprise more than one batch. Each batch should be dealt with separately.

12.12. Each container should be carefully checked for possible contamination, tampering and damage. Any suspect containers or, if necessary, the entire delivery should be quarantined for further investigation.

12.13. Receiving areas should be of sufficient size to allow cleaning of incoming containers.

12.14. When required, samples should be taken only by appropriately trained and qualified personnel and in strict accordance with written sampling procedure and sampling plans. Containers from which samples have been taken should be labelled accordingly.

12.15. Following sampling, the goods should be subject to quarantine. Batch segregation should be maintained during quarantine and all subsequent storage.

12.16. Materials and products requiring storage under controlled conditions of temperature and relative humidity should be handled as a priority.

12.17. Materials and products should remain in quarantine until an authorized release or rejection is obtained.

12.18. Measures should be taken to ensure that rejected materials and products cannot be used. They should be stored separately from other materials and products while awaiting destruction or return to the supplier.

Storage areas

12.19. Precautions should be taken to prevent unauthorized persons from entering storage areas.

12.20. Storage areas should be of sufficient capacity to allow the orderly storage of the various categories of materials and products, such as starting and packaging materials, intermediates, finished products, products in quarantine, and released, rejected, returned or recalled products.

12.21. Storage areas should be appropriately designed, constructed, maintained or adapted. They should be kept clean and dry and there should be sufficient space and lighting.

12.22. Storage areas should be maintained within acceptable temperature limits. Where special storage conditions are required on the label (e.g. temperature, relative humidity), these should be provided, controlled, monitored and recorded.

12.23. Materials and products should be stored off the floor and suitably spaced to permit ventilation, cleaning and inspection. Suitable pallets should be used and kept in a good state of cleanliness and repair.

12.24. A written sanitation programme should be available indicating the frequency of cleaning and the methods to be used to clean the premises and storage areas.

12.25. There should be a written programme for pest control. The pest-control agents used should be safe and there should be no risk of contamination of the materials and products.

12.26. There should be appropriate procedures for the clean-up of any spillage to ensure complete removal of any risk of contamination.

12.27. Where the status is ensured by storage in separate areas, these areas must be clearly marked and their access restricted to authorized personnel. Any system replacing physical separation and labelling or demarcation should provide equivalent security. For example, computerized systems can be used provided that they are validated to demonstrate security of access.

12.28. Where required, a separate sampling area should be in place. If sampling is performed in the storage area, it should be conducted in such a way that there is no risk of contamination or cross-contamination. Adequate cleaning procedures should be in place for the sampling areas.

12.29. Certain materials and products such as highly active and radioactive materials, narcotics and other hazardous, sensitive and/or dangerous materials and products, as well as substances presenting special risks of abuse, fire or explosion (e.g. combustible liquids and solids and pressurized gases), should be stored in a dedicated area that is subject to appropriate additional safety and security measures.

12.30. Materials and products should be handled and stored in such a manner as to prevent contamination, mix-ups and cross-contamination.

12.31. Materials and products should be stored in conditions which assure that their quality is maintained and stock should be appropriately rotated. The “first expired/first out” (FEFO) principle should be followed.

12.32. Rejected materials and products should be identified and controlled under a quarantine system designed to prevent their use until a final decision is taken on their fate.

12.33. Narcotic products should be stored in compliance with international conventions, and national laws and regulations on narcotics.

12.34. Broken or damaged items should be withdrawn from usable stock and separated.

12.35. There should be appropriate proceduresfor the clean-up of any spillage to ensure complete removal of any risk of contamination.

Storage conditions

12.36. The storage conditions for materials and medical products should be in compliance with the labelling, which is based on the results of stability testing.

12.37. Heating, ventilation and air conditioning systems (HVAC) should be appropriately designed, installed, qualified and maintained to ensure that the required storage conditions are maintained.

12.38. Where required, mapping studies for temperature and relative humidity, as appropriate, should be done to show uniformity across the storage facility. (Ref: WHO Technical Report Series No. 961, Annex 9, Model guidance for the storage and transport

of time- and temperature-sensitive pharmaceutical products). This applies, for example, to areas, refrigerators and freezers.

12.39. Temperature and relative humidity, as appropriate, should be controlled and monitored at regular intervals. Data should be recorded and the records should be reviewed. The equipment used for monitoring should be calibrated and be suitable for their intended use. All records pertaining to mapping and monitoring should be kept for a suitable period of time and as required by national legislation.

12.40. Temperature and relative humidity, as appropriate, should be controlled and monitored at regular intervals. Data should be recorded and the records should be reviewed. The equipment used for monitoring should be calibrated and be suitable for their intended use. All records pertaining to mapping and monitoring should be kept for a suitable period of time and as required by national legislation.

Note: See annexure 1 for recommended storage conditions.

13. STOCK CONTROL AND ROTATION

13.1. Periodic stock reconciliation should be performed at defined intervals by comparing the actual and recorded stocks.

13.2. The root cause for stock discrepancies should be identified and appropriate CAPAs taken to prevent recurrence.

13.3. Damaged containers should not be issued unless the quality of the material has been shown to be unaffected. Where possible, this should be brought to the attention of the person responsible for quality. Any action taken should be documented.

13.4. All stocks should be checked regularly for obsolete, to be retested, and expired materials and products.

14. EQUIPMENT

14.1. Equipment, including computerized systems should be suitable for their intended use. These should be appropriately designed, located, installed, qualified and maintained.

14.2. Computerized systems should be capable of achieving the desired output and results.

14.3. Where electronic commerce (e-commerce) is used, i.e. electronic means are used for any of the steps, de?ned procedures and adequate systems should be in place to ensure traceability and con?dence in the supply chain and products concerned.

14.4. Electronic transactions (including those conducted via the Internet) relating to the distribution of medical products should be performed only by authorized persons according to defined and authorized access and privileges.

14.5. Where GXP systems are used, these should meet the requirements of 21 CFR 211 Part 11, EU chapter 11 and WHO guidelines on computerized systems.

14.6. Data should meet ALCOA principles. Procedures should be followed, and records maintained for the back-up and restoration of data.

15. QUALIFICATION AND VALIDATION

15.1. The scope and extent of qualification and validation should be determined using a documented risk assessment approach.

15.2. Premises, utilities, equipment and instruments, processes and procedures should be considered. The scope and extent of qualification and validation in case of any significant changes should be identified.

15.3. Qualification and validation should be done following procedures and protocols. The results and outcome of the qualification and validation should be

recorded in reports. Deviations should be investigated and the completion of the qualification and validation should be concluded and approved by responsible personnel.

16. PERSONNEL

16.1. There should be an adequate number of personnel.

16.2. Personnel should have appropriate educational qualification, experience and training relative to the activities undertaken.

16.3. Personnel should have the authority and resources needed to carry out their duties and to follow the quality systems, as well as to identify and correct deviations from the established procedures.

16.4. There should be arrangements in place to ensure that management and personnel are not subject to commercial, political, ?nancial and other pressures or con?ict of interest that may have an adverse effect on the quality of service provided or on the integrity of pharmaceutical products.

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

16.6. Personnel should receive initial and continued training in accordance with a written training programme. The training should cover the requirements of GSP, GDP (as applicable), as well as on-the-job training Other topics may include product security, product identi?cation, the detection of falsified products.

16.7. 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, ?re or explosion) should be given speci?c training.

16.8. Personnel should be trained in, and observe high levels of, personal hygiene and sanitation.

16.9. Records of all training, attendance and assessment should be kept.

16.10. Personnel handling 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, infectious or sensitizing, should be provided with protective garments as necessary.

16.11. 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.

16.12. Procedures and conditions of employment for employees, including contract and temporary staff, and other personnel having access to medical products, must be designed and administered to assist in minimizing the possibility of such products coming into the possession of unauthorized persons or entities.

16.13. Codes of practice and punitive procedures should be in place to prevent and address situations where persons involved in the storage and distribution of medical products are suspected of, or found to be implicated in, any activities relating to the misappropriation, tampering, diversion or falsifying of any product.

17. DOCUMENTATION

17.1. Documentation includes all procedures and records, whether in paper or electronic form. Documents should be appropriately designed, completed, reviewed, authorized, distributed and kept as required. Documents should be readily available.

17.2. Written procedures should be followed for the preparation, review, approval, use of and control of all documents relating to the policies and activities for storage and distribution of medical products process.

17.3. Documents should be laid out in an orderly fashion and be easy to complete, review and check. The title, scope, objective and purpose of each document should be clear.

17.4. The contents of documents should be accurate, legible, traceable, attributable and unambiguous.

17.5. All documents should be completed, signed and dated as required by authorized person(s) and should not be changed without the necessary authorization.

17.6. Documentation should be prepared and maintained in accordance with the national legislation and principles of good documentation practices (see WHO Technical Report Series No. 996, Annex 5, Guidance on good data and record management practices).

17.7. The distributor must establish and maintain procedures for the identi?cation, collection, indexing, retrieval, storage, maintenance, disposal of and access to all applicable documentation.

17.8. Documents should be reviewed regularly and kept up-to-date. When a document has been revised, a system should exist to prevent inadvertent use of the superseded version.

17.9. All records must be readily retrievable and be stored and retained using facilities that are safeguarded against unauthorized access, modi?cation, damage, deterioration and/or loss of documentation.

17.10. Records should contain at least the following information:

? date;

? name of the product;

? quantity received, or supplied; and

? name and address of the supplier.

17.11. Comprehensive records should be maintained for all receipts, materials and products stored, and issues or distribution. They should include, for example, the description of the goods, quantity, names and addresses (such supplier, customer), batch number(s), date of receipt/dispatch and expiry date.

17.12. All containers should be clearly labelled with at least the name of the material/product, the batch number, the expiry date or retest date, and the specified storage conditions. Unauthorized abbreviations, names or codes should not be used.

18. ACTIVITIES AND OPERATIONS

18.1. All activities and operations relating to procurement, storage and distribution of medical products should be conducted in accordance with national legislation, GSP, GDP and associated guidelines.

18.2. Storage and distribution of medical products should be done by persons so authorized, in accordance with national legislation.

18.3. Activities and operations should be performed in accordance with documented procedures.

Receiving

18.4. Materials and products should be procured from appropriately authorized suppliers.

18.5. Deliveries should be examined for damage, seal intactness, signs of tampering, labelling, completeness of order and other related aspects, at receipt.

18.6. Containers and consignments not meeting acceptance criteria for receiving should be separated, quarantined and investigated. This includes suspected falsified products.

18.7. Materials and products requiring specific storage conditions, or access control (e.g. narcotics) should be processed without delay and stored in accordance with their requirements.

Storage

18.8. There should be sufficient space for the safe and secure storage of medical products (see section xxx above).

18.9. Appropriate controls should be implemented to prevent contamination and/or mix ups during storage.

18.10. Storage areas should be clean and kept free from litter, birds, dust and pests.

18.11. Controls and procedures should be in place to prevent and handle spillage and breakage.

18.12. Materials and products should be stored under the conditions specified on the label, e.g. controlled temperature and relative humidity when necessary. When specific storage conditions are required, the storage area should be qualified and operated within the specified limits. The storage conditions should be monitored and records maintained. The records should be reviewed and trends and out of limit results investigated.

18.13. Stock should be rotated and the FEFO policy should be implemented.

18.14. Computerized systems used for stock management should be validated.

18.15. Materials and products reaching their expiry date should be separated from usable stock and not be supplied.

Repackaging and relabelling

18.16. Repackaging and relabelling of materials and products are not recommended. Where they do occur, they should only be performed by entities appropriately authorized to do so and in compliance with the applicable national, regional and international requirements, and in accordance with GMP.

18.17. Proceduresshould be in place for the controlled disposal of original packaging to prevent re-use.

Distribution and transport

18.18. Materials and products should be transported in accordance with the conditions stated on the labels. There should be no risk to the quality of the material or product during transport and distribution.

18.19. Product, batch and container identity should be maintained at all times.

18.20. All labels should remain legible.

18.21. Distribution records should be sufficiently detailed to allow for a recall when required.

18.22. A copy of the original certificate of analysis from the manufacturer should be provided to the customer.

18.23. Drivers of vehicles should be identified and present appropriate documentation to demonstrate that they are authorized to transport medical products.

18.24. Vehicles should be suitable for their purpose, with sufficient space and appropriately equipped to protect materials and products.

18.25. 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 products.

18.26. Where feasible, consideration should be given to adding technology, such as global positioning system (GPS) electronic tracking devices and engine-kill buttons to vehicles, which would enhance the security and traceability of vehicles with products.

18.27. Where possible, dedicated vehicles and equipment should be used for medical products. Where non-dedicated vehicles and equipment are used, procedures should be in place to ensure that the quality of the products will not be compromised. Defective vehicles and equipment should not be used. These should either be labelled as such or removed from service.

18.28. There should be procedures in place for the operation and maintenance of all vehicles and equipment.

18.29. There should be written programmes and records for cleaning and pest control. Records should be kept. The cleaning and fumigation agents used should not have any adverse effect on product quality.

18.30. Equipment chosen and used for the cleaning of vehicles should not constitute a source of contamination. Agents used for the cleaning of vehicles should be approved by management.

18.31. Appropriate environmental conditions 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 longer, if required by national legislation. Records of monitoring data should be made available for inspection by the regulatory or other oversight body.

18.32. Instruments used for monitoring conditions, e.g. temperature and humidity, within vehicles and containers should be calibrated at regular intervals.

18.33. Where possible, mechanisms should be available to allow for the segregation during transit of rejected, recalled and returned products as well as those suspected as falsified. Such goods should be securely packaged, clearly labelled and be accompanied by appropriate supporting documentation.

18.34. 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.

18.35. Shipment containers should have no adverse effect on the quality of the products and should offer adequateprotection to materials and products. Containers should be labelled indicating, e.g. handling and storage conditions, precautions, contents and source, safety symbols as appropriate.

18.36. Special care should be taken when using dry ice in shipment containers due to safety issues and possible adverse effects on the quality of products.

18.37. 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.

Dispatch

18.38. Products should only be sold and/or distributed to persons or entities that are authorized to acquire such products in accordancewith the applicable national legislation. Written proof of such authorization must be obtained prior to the distribution of products to such persons or entities.

18.39. Dispatch and transportation should be undertaken only after the receipt of a valid order which should be documented.

18.40. There should be documented, detailed procedures for the dispatch of products.

18.41. Records for the dispatch of products should be prepared and should include information such as, but not limited to, date of dispatch; complete business name and address (no acronyms), type of entity responsible for the transportation, telephone number, names of contact persons; 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, i.e. number of containers and quantity per container (if applicable); applicable transport and storage conditions; a unique number to allow identification of the delivery order; and assigned batch number and expiry date (where not possible at dispatch, this information should at least be kept at receipt to facilitate traceability).

18.42. Records of dispatch should contain enough information to enable traceability of the product. Such records should facilitate the recall of a batch of a product, if necessary, as well as the investigation of falsified or potentially falsified products. In addition, the assigned batch number and expiry date of pharmaceutical products should be recorded at the point of receipt to facilitate traceability.

18.43. 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.

18.44. 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.

18.45. 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.

18.46. 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; and
- ? appropriate environmental conditions are maintained, e.g. using cold chain for thermolabile products.

18.47. Written procedures should be in place for investigating and dealing with any failure to comply with storage requirements, e.g. temperature deviations. If a deviation has been noticed during transportation by the person or entity 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.

18.48. Transportation of products containing hazardous substances, or narcotics and other dependence-producing substances, should be transported in safe, suitably designed, secured containers and vehicles. In addition, the requirements of applicable international agreements and national legislation should be met.

18.49. 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.

18.50. 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.

18.51. Products in transit must be accompanied by the appropriate documentation.

19. OUTSOURCED ACTIVITIES

19.1. Any activity relating to the storage and distribution of a medical product which is delegated to another person or entity should be performed by parties appropriately authorized, in accordance with national legislation, and the terms of a written contract.

19.2. There should be a written contract between the parties. The contract should define the responsibilities of each party (contract giver and contract acceptor) and at least the following:

- compliance with this guideline and the principles of GSP and GDP;
- relevant warranty clauses;
- responsibilities of the contractor for measures to avoid the entry of substandard and falsified products into the distribution chain;
- training of personnel;
- conditions of subcontracting subject to the written approval of the contract giver; and
- periodic audits.

19.3. The contract giver should assess the competence of the contract acceptor before entering into an agreement.

19.4. The contract giver should provide all relevant information relating to the material/products to the contract acceptor.

19.5. The contract acceptor should have adequate resources (e.g. premises, equipment, personnel, knowledge, experience, vehicles as appropriate) to carry out the work.

19.6. The contract acceptor should refrain from performing any activity that may adversely affect the materials or products handled.

20. SUBSTANDARD AND FALSIFIED PRODUCTS

20.1. The quality system should include procedures to assist in identifying and handling materials and products that are suspected to be substandard and or falsified.

20.2. Where these materials and products are identified, the holder of the marketing authorization, the manufacturer and the appropriate national and/or international regulatory bodies, as well as other relevant competent authorities, should be informed.

20.3. Such products should be stored in a secure, segregated area and clearly identified to prevent further distribution or sale. Access should be controlled.

20.4. Records should be maintained reflecting the investigations and action taken, such as disposal of the material or products. Falsified materials and products should not re-enter the market.

21. INSPECTION OF STORAGE AND DISTRIBUTION FACILITIES

21.1. Storage and distribution facilities should be inspected by inspectors so authorized in terms of national legislation. This should be done at determined periodic intervals.

21.2. Inspectors should have appropriate educational qualifications, knowledge and experience.

21.3. An inspection should normally be conducted by a team of inspectors.

21.4. Inspectors should assess compliance with national legislation, GSP, GDP and related guidelines (GxP) as appropriate.

21.5. Inspections should cover the premises, equipment, personnel, activities, quality system, qualification and validation, and other related aspects as contained in this guideline.

21.6. An inspection report should be prepared and provided to the inspected entity within 30 days from the last day of the inspection. Observations may be categorized based on risk assessment.

21.7. CAPA for observations listed as non-compliances in the inspection report, with the national legislation and guidelines, should be submitted for review by the inspectors within the defined period as stated by the inspectors.

21.8. Inspections should be closed with a conclusion after the review of the CAPAs.

References and further reading

[Note from Secretariat: the references included in the text will be added here in the final version. Proposals for further reading references are invited.]

ANNEXURE 1. RECOMMENDED STORAGE CONDITIONS

Note: Appropriate conditions should be provided for materials and products during storage and distribution. Conditions should be maintained as stated on their labels from the manufacturers and suppliers, during storage and distribution. Where possible, actual limits should be provided by the manufacturers, such as "Store below 25 °C". Vague statements such as "store at ambient conditions" should be avoided.

Table 1. Recommended limits for descriptive storage conditions[1]

Label description	Recommended limits
Store at controlled room temperature	20 to 25 °C
Store in a cool place	8 to 15 °C
Store in a refrigerator	2 to 8 °C
Store in a freezer	-25 to -10 °C
Store in a dry place	No more than 60% relative humidity
Protect from moisture	No more than 60% relative humidity
Store under ambient conditions	Storage in dry, well-ventilated premises at temperatures of 15–30 °C. Extraneous odours, other indications of contamination, and intense light must be excluded.
Do not store over 30 °C	2 to 30 °C
Do not store over 25 °C	2 to 25 °C
Do not store over 15 °C	2 to 15 °C
Do not store over 8 °C	2 to 8 °C
Do not store below 8 °C	8 to 25 °C
Protect from light	To be provided in light resistant containers. Light level not exceeding 300 lux.
Chilled	Refrigerated

[1]These limits are recommended values, based on pharmacopoeia limits and guidelines

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