World Health Organization

GOOD STORAGE AND DISTRIBUTION PRACTICES FOR MEDICAL PRODUCTS

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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 **20 September 2019**.

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Please send any request for permission to:

Dr Sabine Kopp, Group Lead, Medicines Quality Assurance, Technologies Standards and Norms, Department of Essential Medicines and Health Products, World Health Organization, CH-1211 Geneva 27, Switzerland, email: kopps@who.int.

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SCHEDULE FOR DRAFT WORKING DOCUMENT QAS/19.793:

GOOD STORAGE AND DISTRIBUTION PRACTICES

FOR MEDICAL PRODUCTS

Description of Activity	**Date**
During the Fifty-third WHO Expert Committee on Specifications for Pharmaceutical Preparations (ECSPP), the Expert Committee recommended the consolidation of good storage practices and good distribution practices with elements from the guidelines for inspection of drug distribution channels, into one document.	22-26 October 2018
Preparation of first draft working document.	December 2018 - March 2019
Mailing of working document inviting comments, including to the Expert Advisory Panel on the International Pharmacopoeia and Pharmaceutical Preparations (EAP), 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.	End of June 2019
Discussion of working document and feedbacks received during the public consultation in the informal Consultation on Good Practices for Health Products Manufacture and Inspection.	2-5 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 inviting comments, including to the EAP, and posting the working document on the WHO website for the second round of public consultation.	August – 20 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.	

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GOOD STORAGE AND DISTRIBUTION PRACTICES FOR MEDICAL PRODUCTS

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GOOD STORAGE AND DISTRIBUTION PRACTICES FOR MEDICAL PRODUCTS

1. INTRODUCTION

1.1 Storage and distribution are important activities in the supply chain management of medical products. Various people and entities may be responsible for the handling, storage and distribution of medical products. Medical products may be subjected to various risks at different stages in the supply chain, for example, purchasing, storage, repackaging, relabelling, transportation and distribution.

1.2 Substandard and falsified products are a significant threat to public health and safety. Consequently, it is essential to protect the supply chain against the penetration of such products.

1.3 This document sets out steps to assist in fulfilling 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.

1.4 This guideline is intended to be applicable to all entities involved in any aspect of the storage and distribution of medical products, from the premises of the manufacturer of the medical product to his or her agent, or the person dispensing or providing medical products directly to a patient. This includes all entities involved in different stages of the supply chain of medical products, manufacturers and wholesalers as well as brokers, suppliers, distributors, logistics providers, traders, transport companies and forwarding agents and their employees .

1.5 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 health care workers.

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1.6 This guideline can 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 specific needs and situations in a particular region or country.

1.7 To maintain the 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) (*1*), good storage practices (GSP) (*2*) and good distribution practices (GDP) (*3*), as applicable.

1.8 This guideline does not deal with dispensing to patients as this is addressed in the World Health Organization (WHO) Good Pharmacy Practice (GPP) (*4*).

1.9 This guideline should also be read in conjunction with other WHO guidelines.

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 below.

2.2 Depending on the national and regional legislation, these guidelines may apply equally to medical products for human and veterinary use.

2.3 The document does not specifically cover GMP aspects of finished 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

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laid down in the WHO document Good Trade and Distribution Practices for Pharmaceutical Starting Materials *(5)*.

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.

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broker.

Arranges transactions in relation to the sale or purchase of medical products that consist of negotiating, independently and on behalf of another legal or natural person, and that do not include physical handling.

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 specified price.

corrective and preventative actions (CAPA).

A system for implementing corrective 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 finished pharmaceutical product with another starting material or product during production, storage and transportation.

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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.

falsified product.

A product that has been deliberately and/or fraudulently misrepresented as to its identity, composition or source. Such deliberate/fraudulent misrepresentation refers to any substitution, adulteration, reproduction of an authorized product or the manufacture of a product that is not an authorized product. "Identity" shall refer to the name, labelling or packaging or to documents that support the authenticity of an authorized product. "Composition" shall refer to any ingredient or component of the product in accordance with applicable specifications authorized/ recognized by the NRA. "Source" shall refer to the identification, including name and address, of the marketing authorization holder, manufacturer, importer, exporter, distributor or retailer, as applicable. (*Reference*: Member State mechanism on substandard/spurious/falsely-labelled/falsified/counterfeit medical products. Report by the Director-General; 2017, http://apps.who.int/gb/ebwha/pdf_files/WHA70/A70_23-en.pdf)

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.

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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 falsified, unapproved, illegally imported, stolen, 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 practices (GXP).

Acronym for the group of good practice guides governing the preclinical, clinical, manufacturing, testing, storage, distribution and post-market activities for regulated pharmaceuticals, biologicals and medical devices, such as good laboratory practices (GLP), good clinical practices (GCP), good manufacturing practices (GMP), good pharmacovigilance practices (GPP) and good distribution practices (GDP).

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.

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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 finished 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 national regulatory authority for the purpose of marketing or free distribution of a product after evaluation for safety, efficacy 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

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national generic names where they exist), the shelf life and storage conditions, and packaging characteristics, or other details as required by the product category. It specifies the information on which authorization is based (e.g. "The product(s) must conform to all the details provided in your application and as modified in subsequent correspondence"). It also 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 (APIs and excipients), reagents, solvents, process aids, intermediates, packaging materials and labelling materials.

medical products.

Products including, but not limited to, finished pharmaceutical products, medical devices, vaccines and in vitro diagnostics (IVDs).

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 a pharmaceutical 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 finished dosage form, which is subject to control by pharmaceutical legislation in either the exporting or the importing state and includes products

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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, complaints of serious adverse reactions to the product and/or concerns that the product is or may be falsified. 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 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.

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 confidence 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.

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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 defined purpose, for example, acceptance of consignments or batch release.

self-inspection.

Self-inspection is an internal procedure followed to evaluate the entity's compliance with GSDP and GXP in all areas of activities, designed to detect any shortcomings and to recommend and implement necessary corrective actions.

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. 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.

substandard products.

"Substandard" medical products (also called "out of specification") are authorized by national regulatory authorities but fail to meet either national or international quality standards or specifications – or, in some cases, both.

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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 entities, 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 medical 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:

- medical products moving forward in the distribution chain from the manufacturer;
- medical products which are moving backwards in the chain, for example, as a result of the return or recall thereof; and
- donations of medical products.

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5. QUALITY MANAGEMENT

Quality Systems

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

5.2 Senior management has the ultimate responsibility to ensure that an effective quality system is established, resourced, implemented and maintained.

5.3 The quality system should ensure that:

- GSP and GDP are adopted and implemented to ensure that the quality of medical products is maintained throughout their shelf-life in the supply chain; medical products are appropriately procured, stored, distributed and delivered (in compliance with the legislation) to the appropriate recipients; (see 18.1)
- operations are clearly specified in 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 quality audits;
- there is a system for quality risk management (QRM);
- there are systems for managing returns, complaints and recalls;
- there are systems 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.

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

5.6 Roles and responsibilities should be clearly defined 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 .

6.2 The evaluation of the risk should be based on scientific knowledge and experience and ultimately be linked to the protection of the patient.

6.3 Appropriate controls should be developed and implemented to address all risks. The effectiveness of the controls implemented should be evaluated at periodic intervals.

7. MANAGEMENT REVIEW

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

- 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 Minutes and related documentation from management review meetings should be available.

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8. COMPLAINTS

8.1 There should be a written procedure for the handling of complaints. In the case of a complaint about the quality of a medical 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) risk assessed. Appropriate CAPAs should be taken.

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

8.4 A distinction should be made between complaints about a medical product or its packaging and those relating to distribution.

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

8.6 Medical product quality problems and suspected cases of substandard or falsified products identified should be handled according to relevant authorized procedures. The information should be shared with the manufacturer and appropriate national and/or regional regulatory authorities without delay .

9. RETURNED GOODS

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

9.2 All returned medical products should be placed in quarantine upon receiving. The status of the goods should be clear. Precautions should be taken to prevent access and

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distribution until a decision has been taken with regard to their disposition. The particular storage conditions applicable to the medical products should be maintained.

9.3 Medical products returned should be destroyed unless it is certain that their quality is satisfactory after they have been critically assessed in accordance with a written and authorized procedure.

9.4 The nature of the medical product, any special storage conditions it requires, its condition and history and the time lapse since it was issued, should all be taken into account in this assessment. Where any doubt arises over the quality of the medical product, it should not be considered suitable for reissue or reuse. Any action taken should be appropriately recorded.

9.5 When handling returned goods, the following considerations at least 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 and the manner and condition of transport while being returned.
- The terms and conditions of the agreement between the parties.
- Examination of the returned goods, with decisions taken by suitably qualified, experienced and authorized persons.

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

9.7 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.

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9.8 Records of all returned, rejected and destroyed medical products should be kept for a defined period in accordance with national requirements.

10. RECALLS

10.1 There should be a written procedure, in compliance with national or regional requirements, to effectively and promptly recall medical products.

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 secure, segregated, transported and stored under appropriate conditions. These should be 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 medical 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 sufficient information on products supplied to customers (e.g. name, address, contact detail, batch numbers, quantities and safety features - including exported products).

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

11. SELF-INSPECTION

11.1 The quality system should include self-inspections. These should be conducted to monitor the implementation, compliance with and effectiveness of SOPs as well as compliance with 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

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 and 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.

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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 conditions such as radioactive 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 should 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, for example, the purchase order, containers, label description, batch number, expiry date, 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

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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 the cleaning of incoming medical products.

12.14 When required, samples of medical products should be taken by appropriately trained and qualified personnel and in strict accordance with a 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, as applicable, should be handled as a priority.

12.17 Medical products should not be transferred to saleable stock until an authorized release is obtained.

12.18 Measures should be taken to ensure that rejected medical products cannot be used. They should be segregated and securely stored while awaiting destruction or return to the supplier.

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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 medical products.

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

12.22 Storage areas should be maintained within acceptable and specified 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 Medical 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 appropriate procedures for the clean-up of any spillage to ensure complete removal of any risk of contamination.

12.26 Where the status is ensured by storage in separate areas, these areas should 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 (*6*).

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12.27 Sampling should be done under controlled conditions and conducted in such a way that there is no risk of contamination or cross-contamination. Adequate cleaning procedures should be followed after sampling.

12.28 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; and in accordance with national legislation

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

12.30 Medical products should be stored in conditions which assure that their quality is maintained. Stock should be appropriately rotated. The "first expired/first out" (FEFO) principle should be followed.

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

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

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

Storage conditions

12.34 The storage conditions for medical products should be in compliance with their labelling.

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12.35 Heating, ventilation and air conditioning systems (HVAC) should be appropriately designed, installed, qualified and maintained to ensure that the required storage conditions are maintained (*7*).

12.36 Mapping studies for temperature and relative humidity, as appropriate, should be done (*8*). This applies, for example, to areas, refrigerators and freezers.

12.37 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 Annex 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 stock.

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

13.3 When damaged containers are received, this should be brought to the attention of the person responsible for quality. Any action taken should be documented. (These containers should not be issued unless the quality of the medical products has been shown to be unaffected).

13.4 All stock should be checked regularly to identify obsolete, to be retested, and expired stock.

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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 for any of the steps, defined procedures and adequate systems should be in place to ensure traceability and confidence 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 WHO and other guidelines on computerized systems (6,9).

15. QUALIFICATION AND VALIDATION

15.1 The scope and extent of qualification and validation should be determined using documented risk management principles.

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.

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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 subjected 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 medical products.

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

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 should be included, such as product security, product identification and the detection of falsified products.

16.7 Personnel dealing with hazardous 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.

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

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16.9 Records of all training, attendance and assessments 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 the 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 implemented 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, records and data, 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.

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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 (*9*).

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

17.8 The distributor must establish and maintain procedures for the identification, collection, indexing, retrieval, storage, maintenance, disposal of and access to all applicable documentation.

17.9 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.

17.10 All records should be stored and retained using facilities that prevent unauthorized access, modification, damage, deterioration and/or loss of documentation during the entire life cycle of the record. Records must be readily retrievable.

17.11 Comprehensive records should be maintained for all receipts, storage, issues and distribution. The records should include, for example:

- date (e.g. receipt or dispatch, as appropriate);
- name and description of the product;
- quantity received, or supplied;
- name and address of the supplier and customer.
- batch number(s);
- expiry date;

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- suitability of the supplier;
- qualification of suppliers; and
- customer qualification.

17.12 All containers should be clearly labelled with at least the name of the medical product, batch number, expiry date or retest date, and the specified storage conditions.

18. ACTIVITIES AND OPERATIONS

18.1 All activities and operations 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.

18.4 Automated Storage and Retrieval Systems (AS/RS) and operations should comply with current GSP, GDP and GXP guidelines, as well as the recommendations in this guideline.

Receiving

18.5 Medical products should be procured from appropriately authorized suppliers.

18.6 Deliveries should be examined for damage, seal intactness, signs of tampering, labelling, completeness of order and other related aspects, at the time of receiving.

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18.7 Containers and consignments not meeting acceptance criteria at the time of receipt should be labelled, kept separate and investigated. This includes suspected falsified products.

Storage

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

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

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

Repackaging and relabelling

18.11 Repackaging and relabelling of materials and products are not recommended. Where repackaging and relabelling occur, these activities 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.

18.12 Procedures should be in place for the controlled disposal of original packaging to prevent re-use thereof.

Distribution and transport

18.13 Medical products should be transported in accordance with the conditions stated on the labels. There should be no risk to the quality of the medical product during transport and distribution.

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

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18.15 All labels should remain legible.

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

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

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

18.19 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.

18.20 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.

18.21 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.

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

18.23 Equipment and materials used for the cleaning of vehicles should not become a source of contamination or have an adverse effect on product quality.

18.24 Appropriate environmental conditions should be maintained, monitored and recorded. All monitoring records should be kept for a defined period of time as required by

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national legislation. Records of monitoring data should be made available for inspection by the regulatory or other oversight body.

18.25 Instruments used for monitoring conditions, for example, temperature and humidity, within vehicles and containers should be calibrated at regular intervals.

18.26 Rejected, recalled and returned products, as well as those suspected as being falsified, should be securely packaged, clearly labelled and be accompanied by the appropriate supporting documentation.

18.27 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.

18.28 Shipment containers should have no adverse effect on the quality of the medical products and should offer adequate protection to materials and these products. Containers should be labelled indicating, for example, handling and storage conditions, precautions, contents and source, and safety symbols, as appropriate.

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

18.30 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

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

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18.32 Medical 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 legislation. Written proof of such authorization must be obtained prior to the distribution of products to such persons or entities.

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

18.34 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, for example, 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).

18.35 Records of dispatch should contain sufficient 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 products should be recorded at the point of receipt to facilitate traceability.

18.36 Vehicles and containers should be loaded carefully and systematically on a last-in/first-out (LIFO) to save time when unloading, to prevent physical damage and to reduce

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security risks. Extra care should be taken during loading and unloading of cartons to avoid damage.

18.37 Medical 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 (*10*).

18.38 Medical products and shipment containers should be secured in order to prevent or to provide evidence of unauthorized access. Vehicles and operators should be provided with additional security where necessary, to prevent theft and other misappropriation of products during transportation.

18.39 Medical 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, for example, using cold chain for thermolabile products.

18.40 Written procedures should be in place for investigating and dealing with any failure to comply with storage requirements, for example, 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.

18.41 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.

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18.42 Spillages should be cleaned up as soon as possible in order to prevent possible contamination, cross-contamination and hazards. Written procedures should be in place for the handling of such occurrences.

18.43 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.

18.44 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 the 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 entities. The contract should define the responsibilities of each entity (contract giver and contract acceptor) and cover at least the following:

- compliance with this guideline and the principles of GSP and GDP;
- responsibilities of all entities 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 the contract.

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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 and 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 medical products that are suspected to be substandard and/or falsified.

20.2 Where such medical products are identified, the holder of the marketing authorization, the manufacturer and the appropriate national, regional and international regulatory bodies (as appropriate), 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 product. Falsified 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 by national legislation. This should be done at determined, periodic intervals.

21.2 Inspectors should have appropriate educational qualifications, knowledge and experience (*11*).

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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 a defined period of time 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

1. WHO Good Manufacturing Practices for Pharmaceutical Products: Main Principles (WHO Technical Report Series, No. 986, 2014, Annex 2).

2. WHO Guide to Good Storage Practices for Pharmaceuticals (WHO Technical Report Series, No. 908, 2003, Annex 9). [*under revision*]

3. Good Distribution Practices for Pharmaceutical Products (WHO Technical Report Series, No. 957, 2010, Annex 5). [*under revision*]

4. Good Pharmacy Practice: Standards for Quality of Pharmacy Services (joint FIP/WHO) (WHO Technical Report Series, No. 961, 2011, Annex 8).

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5. Good Trade and Distribution Practices for Starting ;aterials (WHO Technical Report Series, No. 996, 2016, Annex 6).

6. Validation of Computerized Systems (WHO Technical Report Series, No. 1019, 2019, Annex 5).

7. Guidelines on Heating, Ventilation and Air-Conditioning Systems for Non-Sterile Pharmaceutical Products (WHO Technical Report Series, No. 1019, 2019, Annex 2).

8. Model Guidance for the Storage and Transport of Time- and Temperature-Sensitive Pharmaceutical Products (WHO Technical Report Series, No. 961, Annex 9).

9. Guidance on Good Data and Record Management Practices (WHO Technical Report Series, No. 996, 2016, Annex 5).

10. WHO Policy on Remaining Shelf Life of Medical Products (working document QAS/19.788).

11. Quality Systems Requirements for National Inspectorates (working document QAS/19.811/Rev.1).

Further reading

1. WHO Guidelines on Quality Risk Management (WHO Technical Report Series, No. 981, 2013, Annex 2).

2. Quality Risk Management, ICH Q9, 2015.

3. Risk Management – Guidelines. ISO 31000:2018.

4. Medical Devices – Application of Risk Management to Medical Devices. ISO 14971:2018.

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5. Medical Devices – Quality Management Systems – Requirements for Regulatory Purposes. ISO 13485:2016.

6. WHO Guidance on Testing of "Suspect" Falsified Medicines (WHO Technical Report Series, No. 1010, 2018, Annex 5).

7. Guidelines on Import Procedures for Pharmaceutical Products (WHO Technical Report Series, No. 1019, 2019, Annex 5).

8. Good Practices of National Regulatory Authorities in Implementing the Collaborative Registration Procedures for Medical Products (WHO Technical Report Series, No. 1019, 2019, Annex 6).

9. Guidelines for Medicine Donations, 3rd edition 2011. https://apps.who.int/iris/bitstream/handle/10665/44647/9789241501989_eng.pdf?sequence=1

10. Guidelines for Safe Disposal of Unwanted Pharmaceuticals in and after Emergencies: Interagency Guidelines. Geneva, World Health Organization, 1999 (WHO/EDM/PAR/99.2).

11. Model quality assurance system for procurement agencies (WHO Technical Report Series, No 986, 2014, Annex 3).

12. Validation (WHO Technical Report Series, No 1019, 2019, Annex 3).

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ANNEX 1

RECOMMENDED STORAGE CONDITIONS

Note: Appropriate conditions should be provided for medical products during storage and distribution. Conditions should be maintained as stated on their labels from the manufacturers and suppliers during storage and distribution. Statements such as "store at ambient conditions" should be avoided. Where possible, actual limits should be specified by the manufacturers, such as "store below 25ºC". See Table 1 below.

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

Label description	Recommended limits
Store at controlled room temperature	15 to 25 °C
Store in a cold or cool place	8 to 15 °C
Store in a refrigerator	5 ± 3 °C
Store in a freezer	-20 ± 5 °C
Store in deep freezer	Below -15 °C or -70 ±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	Store in dry, well-ventilated premises at temperatures of between 15 –30 °C. Extraneous odours, other indications of contamination and intense light must be excluded.
Protect from light	To be provided in light resistant containers. Light level not exceeding 500 lux.
Chilled	Refrigerated

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

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