Republic of the Philippines
Department of Health
OFFICE OF THE SECRETARY

OCT 0 2 2013

ADMINISTRATIVE ORDER
No. 2013 - 0027

SUBJECT : Adoption and Implementation of the World Health Organization Annex 5 Guide to Good Distribution Practices (GDP) for Pharmaceutical Products, and Annex 9 Guide to Good Storage Practices for Pharmaceuticals

I. RATIONALE

In order to maintain the original quality of the product, every activity in the distribution of pharmaceutical products should be carried out in the principles of Good Manufacturing Practice (GMP), Good Storage Practice (GSP) and Good Distribution Practice (GDP).

The Mutual Recognition Agreement (MRA) created by the ASEAN member States adopted the Pharmaceutical Inspectorate Cooperation Scheme - Good Manufacturing Practice (PIC/s-GMP) as a standard for inspection. Originally, the PIC/s-GMP Guide was derived from the WHO-GMP Guide and was further developed in order to comply with stringent manufacturing and health requirements in PIC/S countries, to cover new areas (e.g. biologicals, radiopharmaceuticals, etc.) and to adapt to the changing scientific and industrial technology (e.g. biotech, parametric release etc.). The aim of such improvements was to ensure that high quality medicines were produced in line with the PIC Convention and then the PIC Scheme.

In order to align with the international level of standard for GMP, Administrative Order No. 2012-0008, "Adoption and Implementation of the Pharmaceutical Inspection Cooperation Scheme (PIC/S) Guides for the Good Manufacturing Practice for Medicinal Products" was issued by FDA.

The World Health Organization (WHO) Annex 5 Guide to Good Distribution Practice (GDP) and Annex 9 Guide to Good Storage Practices (GSP)

for Pharmaceutical Products serve as the standards for the different aspects of the distribution and storage processes for pharmaceutical products.

The FDA, consistent with the 1987 Philippine Constitution Sec. 12 Article XIII, which states that "the state shall establish and maintain an effective food and drug regulatory system", and pursuant to the provisions of Republic Act No. 9711, otherwise known as Food and Drug Administration (FDA) Act of 2009, Sec. 3, which declares a policy of the State "to adopt, support, establish, institutionalize, improve and maintain structures, processes, mechanisms, measures and initiatives that are aimed, directed and designed to: (a) protect and promote the right to health of the Filipino people; and (b) help establish and maintain an effective health products regulatory system responsive to the country's health needs and problems", has crafted and implemented several issuances in order to enhance its regulatory policy and strengthen its capability with regards to the proper storage and distribution of pharmaceutical products. However, these issuances are not equivalent to standards set by the WHO in the international level. This Order is hereby issued for the effective adoption and implementation of the aforementioned WHO guidances.

II. OBJECTIVES

GENERAL OBJECTIVE

To officially adopt and implement the World Health Organization "Annex 5 Guide to Good Distribution Practices (GDP) for Pharmaceutical Products" and "Annex 9 Guide to Good Storage Practices for Pharmaceuticals", attached as Annex A and Annex B, respectively.

SPECIFIC OBJECTIVES

1. To use the WHO Annex 5 Guide to Good Distribution Practices (GDP) for Pharmaceutical Products and Annex 9 Guide to Good Storage Practices for Pharmaceuticals as the standard in assessing GDP and GSP compliance of drug establishments and retailers.
2. To have a coordinated transition period for the FDA and the Drug Establishment from the previous guidelines to the WHO GDP and GSP Guide

III. SCOPE

This Order shall apply to FDA and Drug Establishments and Retailers.

IV. DEFINITION OF TERMS

1. "Authorization" means a permission embodied in a document granted by the FDA to a natural or juridical person who has submitted an application to implement the manufacture, importation, exportation, sale, offer for sale, distribution, transfer, and/or, where appropriate, the use, testing, promotion, advertising, or sponsorship of health products. The authorization can take the form of a permit, a license, a certificate of registration, of accreditation, of compliance, or of exemption, or any similar document.

2. "Distributor/importer/exporter" means any establishment that imports or exports raw materials, active ingredients and/or finished products for its own use or for wholesale distribution to other establishments or outlets. If the distributor/importer/exporter sells to the general public, it shall be considered a retailer.

3. "Distributor/wholesaler" means any establishment that procures raw materials, active ingredients and/or finished products from local establishments for local distribution on wholesale basis.

4. "Drug" means

   (a) Articles recognized in the official pharmacopoeias and formularies, including official homeopathic pharmacopoeias or any documentary supplement to any of them, which are recognized and adopted by the FDA
   (b) Articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals;
   (c) Articles (other than food) intended to affect the structure of any function of the body of humans or animals; or
   (d) Articles intended for use as a component of any articles specified in clauses (1), (2), or (3) but do not include devices or their components, parts or accessories

5. "Drug Establishment" refers to drug manufacturers/repackers, drug importers, drug distributors, drug wholesaler or drug exporter and entities belonging to definition of establishment, as per RA 9711 and its implementing rules and regulations "Establishment" means a sole proprietorship, a partnership, a corporation, an institution, an association, or an organization engaged in the manufacture, importation, exportation, sale, offer for sale, distribution, donation, transfer, use, testing, promotion, advertising, or sponsorship of health products including the facilities and installations needed for its activities.

6. "Good Distribution Practices" or "GDP" means that part of quality assurance which ensures that the quality of a pharmaceutical product is maintained through adequate control throughout the numerous activities which occur during the distribution process.

7. "Good Manufacturing Practice" or "GMP" means that part of quality assurance which ensures that medicinal products are consistently produced and controlled in accordance with quality standards appropriate for their intended use and as required by the applicable marketing authorization or product specifications.

8. "Good Storage Practices" or "GSP" means that part of quality assurance which ensures that the quality of a pharmaceutical product is maintained through adequate control throughout the storage.

9. "Retailer" means any establishment which sells or offers to sell any health product directly to the general public."

V. GENERAL GUIDELINES

The Department of Health (DOH) – FDA hereby adopts the current version of WHO Annex 5 Guide to Good Distribution Practices (GDP) for Pharmaceutical Products and Annex 9 Guide to Good Storage Practices for Pharmaceuticals to supplement A.O. 56 s. 1989 and other related RAs.

VI. SPECIFIC GUIDELINES

1. Supplements and Revisions

   All supplements and revisions related to the WHO Annex 5 Guide to Good Distribution Practices (GDP) for Pharmaceutical Products and Annex 9 Guide to Good Storage Practices for Pharmaceuticals shall be adopted automatically.

2. Accessibility

   The adopted guides shall be made accessible at the FDA Website.

3. Inspection of Drug Establishments and Retailers

   Drug establishments and retailers will be inspected using the WHO GDP and GSP guides as the standard for Good Distribution and Good Storage Practices.

4. Revision of Forms and Templates

   The forms and templates of the Food and Drug Administration shall be revised to reflect the adopted WHO GDP and GSP guides.

5. Capacity Building

   The FDA and the industry shall provide trainings and workshops and may create technical working group/s for the effective implementation of the WHO GDP and GSP guides.

VII. TRANSITORY PROVISIONS

The establishments shall be given a 1-year transition period to comply with the WHO Annex 5 Guide to Good Distribution Practices (GDP) for Pharmaceutical Products and Annex 9 Guide to Good Storage Practices for Pharmaceuticals starting from the effectivity date of this Order.

VIII. PENALTY

The existing administrative and legal sanctions shall be imposed to any person, judicial or natural, who have violated any provisions of this Order, or other regulations referring/related to the licensing of drug establishments including retail outlets.

Unless subsequently amended or superseded, the existing penalties in relation to violation of Good Distribution and Storage Practice shall remain in full force and effect.

IX. SEPARABILITY CLAUSE

If any of the provisions of this administrative order is found by a court of competent jurisdiction to be void or unenforceable, in whole or in part, such provision shall be deemed deleted from this Order but the remaining provisions thereof shall remain in full force and effect.

X. REPEALING CLAUSE

All provisions of existing administrative orders, circulars, regulations and other issuances inconsistent with this Order are hereby repealed or amended accordingly.

XI. EFFECTIVITY DATE

This Order shall take effect after fifteen (15) days following its publication in a newspaper of national circulation and upon submission to the University of the Philippines Law Center.

ENRIQUE T. ONA, MD
Secretary of Health

ANNEX A

World Health Organization
WHO Technical Report Series, No. 937, 2006

Annex 5

Good distribution practices for pharmaceutical products

1. Introduction

Distribution is an important activity in the integrated supply-chain management of pharmaceutical products. Various people and entities are generally responsible for the handling, storage and distribution of such products. In some cases, however, a person or entity is only involved in and responsible for certain elements of the distribution process. This document sets out appropriate steps to assist in fulfilling the responsibilities involved in the different aspects of the distribution process. The guidelines are intended to apply to all steps in the distribution/supply chain. The relevant sections should be considered by various role players as applicable to their particular role in the distribution process. The document does not specifically cover

finished products in bulk, distribution of labels or packaging materials, as these aspects are considered to be covered by other guidelines, e.g. good manufacturing practices (GMP).

The practice of repacking, e.g. in pharmacies and other settings, needs to be carried out in accordance with good dispensing practices.
The storage, trade and distribution of pharmaceutical products are carried out by various companies, institutions and individuals. The nature of the risks involved, however, is likely to be the same as those in the manufacturing environment, e.g. mix-ups, contamination and cross-contamination. There are thus aspects of distribution to which the principles of GMP should be applied. These include, but are not limited to, storage, distribution, transportation, packaging, labelling, documentation and record-keeping practices.
The quality of pharmaceutical products can be affected by a lack of adequate control over the numerous activities which occur during the distribution process. Furthermore the need for establishment, development, maintenance and control over the activities involved in the distribution process has generally not been well emphasized. The objective of these guidelines is to assist in ensuring the quality and integrity of pharmaceutical products during all aspects of the distribution process.

To maintain the original quality of pharmaceutical products, every activity in the distribution thereof should be carried out according to the principles of GMP, good storage practice (GSP) and good distribution practice (GDP). Although these guidelines are intended to be a stand-alone text, they do not deal with all aspects of the standards for the storage of pharmaceuticals which are covered in the "WHO guide to good storage practices for pharmaceuticals" (*1*). These guidelines should also be read in conjunction with other guidelines such as "WHO good manufacturing practices: main principles" (*2*); "Guidelines for implementation of the WHO Certification Scheme on the quality of pharmaceutical products moving in international commerce (*3*); "WHO pharmaceutical starting materials certification scheme (SMACS)" (*4*); and the "Guidelines on import procedures for pharmaceutical products" (*5*).

2. **Scope of the document**

This document lays down guidelines for the distribution of pharmaceutical products. Depending on the national and regional legislation on pharmaceuticals, this guide may also be applicable for veterinary products administered to food-producing animals.

This document does not cover the distribution of materials such as pharmaceutical starting materials (active pharmaceutical ingredients (API) and

excipients), reagents, solvents, process aids, intermediate products, packaging materials and labelling materials. The principles for the distribution of starting materials were laid down in the WHO guidance "Good trade and distribution practices for pharmaceutical starting materials" (*6*).

Different models for the distribution of pharmaceutical products are used in different countries and sometimes within the same country, for example, in the public and the private sector. These guidelines are intended to be applicable to all persons and companies involved in any aspect of the distribution of pharmaceutical products from the premises of manufacture to the point of supply to health establishments, e.g. private pharmacies, hospitals and clinics, for supply to patients. This includes all parties involved in trade and distribution, pharmaceutical manufacturers, including the manufacturers of fi nished products, brokers, suppliers, distributors, wholesalers, traders, transport companies and forwarding agents. The relevant sections of the guidelines should also be considered for implementation by, among others, governments, regulatory bodies, international organizations and donor agencies, certifying bodies, as well as all parties including health care workers involved in any aspect of the trade and distribution of pharmaceutical products. The guidelines can also be used as a tool in the prevention of the distribution of counterfeit and substandard medicines. It should, however, be noted that these are general guidelines which may be adapted to suit the prevailing situations and conditions in individual countries.

3. **Glossary**

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

agreement
Arrangement undertaken by and legally binding on parties.

auditing
An independent and objective activity designed to add value and improve an organization's operations by helping an 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 (*adapted from GMP*).

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

consignment (or delivery)
The quantity of pharmaceutical products supplied at one time in response to a particular request or order. A consignment may comprise one or more packages or containers and may include material belonging to more than one batch (*adapted from GMP*).

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 transport.

contract
Business agreement for the supply of goods or performance of work at a specified price.

counterfeit
A counterfeit medicine is one which is deliberately and fraudulently mislabelled with respect to identity and/or source. Counterfeiting can apply to both branded and generic products and counterfeit products and may include products with the correct ingredients or with the wrong ingredients, without active ingredients, with insufficient active ingredients or with fake packaging.

cross-contamination
Contamination of a starting material, intermediate product or fi nished product with another starting material or product during production.

distribution
The division and movement of pharmaceutical products from the premises of the manufacturer of such products, or another central point, to the end user thereof, or to an intermediate point by means of various transport methods, via various storage and/or health establishments.

excipient
A substance or compound, other than the active pharmaceutical ingredient and packaging materials, that is intended or designated to be used in the manufacture of a pharmaceutical product.

expiry date
The date given on the individual container (usually on the label) of a product up to and including 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.

first expiry/fi 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; earliest expiry/fi rst out (EEFO) has a similar meaning.

first in/fi rst out (FIFO)
A distribution procedure to ensure that the oldest stock is distributed and/or used before a newer and identical stock item is distributed and/or used.

good distribution practices (GDP)
Good distribution practices are 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 throughout the distribution process.

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 storage practices (GSP)
Good storage practices are 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)
Good trade and distribution practices are 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.
health establishment
A health establishment is the whole or part of a public or private facility, building or place, whether operated for profi t or not, that is operated or de-

signed to provide health care services including the supply of pharmaceutical products to the end user.

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 product.

labelling
Process of identifying a pharmaceutical product including the following information, as appropriate: name; 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 (*adapted from GMP*).

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

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

pharmaceutical product
Any medicine intended for human use or veterinary product administered to food-producing animals, presented in its fi nished dosage form, that is subject to control by pharmaceutical legislation in both the exporting state and the importing state (*adapted from GMP*).

product recall
Product recall is a process for withdrawing or removing a pharmaceutical product from the pharmaceutical distribution chain because of defects in the product or complaints of serious adverse reactions to the product. The recall might be initiated by the manufacturer, importer, distributor or a responsible agency.
quality assurance
Quality assurance is 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 control
Quality control covers all measures taken, including the setting of specifi - cations, sampling, testing and analytical clearance, to ensure that starting materials, intermediates, packaging materials and fi nished pharmaceutical products conform with established specifications for identity, strength, purity and other characteristics.

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 (*adapted from GMP*).

sampling
Operations designed to obtain a representative portion of a pharmaceutical product, based on an appropriate statistical procedure, for a defined 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 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 specifi c 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). Certain SOPs may be used to supplement product-specifi c master and batch production documentation.

storage
The storing of pharmaceutical products up to the point of use.
supplier
Person or company providing pharmaceutical products on request. Suppliers include distributors, manufacturers or traders.

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.

validation
Action of proving and documenting that any process, procedure or method actually and consistently leads to the expected results.

vehicle
Vehicle refers to trucks, vans, buses, minibuses, cars, trailers, aircraft, railway carriages, boats and other means which are used to convey pharmaceutical products.

4. **Organization and management**

4.1 The distributor or the organization to which the distributor belongs must be an entity that is appropriately authorized to perform the intended function in terms of the applicable legislation, and which can be held accountable for its activities.

4.2 There should be an adequate organizational structure defined with the aid of an organizational chart. The responsibility, authority and interrelationships of all personnel should be clearly indicated.

4.3 A designated person should be appointed at each distribution point who should have defined authority and responsibility for ensuring that a quality management system is implemented and maintained.

4.4 Managerial and technical personnel must have the authority and resources needed to carry out their duties and to set up and maintain a quality management system, as well as to identify and correct deviations from the established quality management system.
4.5 The responsibilities placed on any one individual should not be so extensive as to present any risk to product quality.
4.6 There should be arrangements in place to ensure that management and personnel are not subject to commercial, political, fi nancial and other pressures or conflicts of interest that may have an adverse effect on the quality of service provided.
4.7 Individual responsibilities should be clearly defined and understood by the individuals concerned and recorded as written job descriptions. Certain activities may require special attention such as the supervision of performance of activities, in accordance with local legislation.
4.8 Some duties may be delegated or contracted out to suitably designated persons or entities as necessary. There should, however, be no gaps or

unexplained overlaps with regard to the application of GDP. These activities should be documented in quality agreements or contracts. There should be periodic audit of such activities with regards to application of GDP.

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

5. **Personnel**

5.1 All personnel involved in distribution activities should be trained in the requirements of GDP and be capable of meeting these requirements.

5.2 Key personnel involved in the distribution of pharmaceutical products should have the ability and experience appropriate to their responsibility for ensuring that pharmaceutical products are distributed properly.

5.3 There should be an adequate number of competent personnel involved in all stages of the distribution of pharmaceutical products in order to ensure that the quality of the product is maintained.

5.4 National regulations with regard to qualifications and experience of personnel should be complied with.

5.5 Personnel should receive initial and continuing training relevant to their tasks, and be assessed as applicable, in accordance with a written training programme.

5.6 Personnel dealing with hazardous pharmaceutical products (such as highly active, and radioactive materials, narcotics, and other hazardous, sensitive and/or dangerous pharmaceutical products, as well as products presenting special risks of abuse, fi re or explosion) should be given specifi c training.
5.7 Records of all training should be kept.
5.8 Personnel involved in the distribution of pharmaceutical products should wear working or protective 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.
5.9 Appropriate procedures relating to personnel hygiene, relevant to the activities to be carried out, should be established and observed. Such procedures should cover health, hygiene and clothing of personnel.
5.11 Procedures and conditions of employment for employees, including contract and temporary staff, and other personnel having access to pharma-

ceutical products must be designed and administered to assist in minimizing the possibility of such products coming into unauthorized possession.
5.12 Codes of practice and disciplinary procedures should be in place to prevent and address situations where persons involved in the distribution of pharmaceutical products are suspected of, or found to be implicated in, the misappropriation and/or theft thereof.

6. **Quality management**

6.1 Within an organization, quality assurance serves as a management tool. In contractual situations quality assurance also serves to generate confidence in the supplier. There should be a documented quality policy describing the overall intentions and policies of the distributor regarding quality, as formally expressed and authorized by management.

6.2 Quality management should include:
— an appropriate infrastructure or "quality system", encompassing the organizational structure, procedures, processes and resources; and
— systematic actions necessary to ensure adequate confidence that a product (or service) and documentation will satisfy given requirements for quality. The totality of these actions is termed "quality assurance".

6.3 The system should at least cover the main principles of quality assurance as embodied in the WHO guidelines on GMP for pharmaceutical products.

6.4 All parties involved in the distribution of pharmaceutical products should share responsibility for the quality and safety of products to ensure that they are fi t for their intended use.

6.5 Where electronic commerce (e-commerce) is used, defined procedures and adequate systems should be in place to ensure traceability and confidence in the quality of pharmaceutical products.

6.6 Authorized procurement and release procedures should be in place, to ensure that appropriate pharmaceutical products are sourced from approved suppliers and distributed by approved entities.

6.7 All entities in the supply chain should be traceable as applicable, depending on the type of product, and on the national policies and legislation.
There should be written procedures and records to ensure traceability of the products distributed.
6.8 Inspection and certification of compliance with a quality system (such as the applicable International Standardization Organization (ISO) series, or national or international guidelines) by external bodies is recommended. Such certification should not, however, be seen as a substitute for

compliance with these guidelines and the applicable principles of GMP relating to pharmaceutical products.

6.9 Authorized SOPs for all administrative and technical operations performed should be in place.

7. **Premises, warehousing and storage**

7.1 Good storage practice (GSP) is applicable in all circumstances where pharmaceutical products are stored and throughout the distribution process. For additional guidance relating to the general principles of storage of pharmaceutical products, refer to the WHO guideline on good storage practices (*1*).

Storage areas

7.2 Precautions must be taken to prevent unauthorized persons from entering storage areas.

7.3 Storage areas should be of sufficient capacity to allow the orderly storage of the various categories of pharmaceutical products, namely bulk and fi nished products, products in quarantine, and released, rejected, returned or recalled products.

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

7.5 Storage areas should be clean, and free from accumulated waste and vermin. 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. There should also be a written programme for pest control. The pest-control agents used should be safe, and there should be no risk of contamination of pharmaceutical products. There should be appropriate procedures for the clean up of any spillage to ensure complete removal of any risk of contamination.

7.6 If sampling is performed in the storage area, it should be conducted in such a way as to prevent contamination or cross-contamination. Adequate cleaning procedures should be in place for the sampling areas.

7.7 Receiving and dispatch bays should protect products from the weather. Reception areas should be designed and equipped to allow incoming containers of pharmaceutical products to be cleaned, if necessary, before storage.

7.8 Where quarantine 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 quarantine should provide equivalent security. For example, computerized systems can be used, provided that they are validated to demonstrate security of access.

7.9 Physical or other equivalent validated (e.g. electronic) segregation should be provided for the storage of rejected, expired, recalled or returned products. The products and areas concerned should be appropriately identifi ed.

7.10 Radioactive materials, narcotics and other hazardous, sensitive and/ or dangerous pharmaceutical products, as well as products presenting special risks of abuse, fi re or explosion (e.g. combustible liquids and solids and pressurized gases) should be stored in a dedicated areas that are subject to appropriate additional safety and security measures.

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

7.12 A system should be in place to ensure that pharmaceutical products due to expire fi rst are sold and/or distributed fi rst (FEFO). Where no expiry dates exist for the products, the FIFO principle should be applied. Exceptions may be permitted as appropriate, provided that adequate controls are in place to prevent the distribution of expired products.

7.13 Rejected pharmaceutical products should be identified and controlled under a quarantine system designed to prevent their use until a fi nal decision is taken on their fate.
7.14 Narcotic drugs should be stored in compliance with international conventions, and national laws and regulations on narcotics.
7.15 Broken or damaged items should be withdrawn from usable stock and stored separately.
7.16 Storage areas should be provided with adequate lighting to enable all operations to be carried out accurately and safely.

Storage conditions

7.17 Storage conditions for pharmaceutical products should be in compliance with the instructions on the label, which are based on the results of stability testing.

Monitoring of storage conditions
7.18 Recorded temperature monitoring data should be available for review. The equipment used for monitoring should be checked at suitable predetermined intervals and the results of such checks should be recorded and retained. All monitoring records should be kept for at least the shelf-

life of the stored pharmaceutical product plus one year, or as required by national legislation. Temperature mapping should show uniformity of the temperature across the storage facility. It is recommended that temperature monitors be located in areas that are most likely to show fluctuations.
7.19 Equipment used for monitoring of storage conditions should also be calibrated at defined intervals.

Stock rotation and control

7.20 Periodic stock reconciliation should be performed by comparing the actual and recorded stocks.
7.21 All significant stock discrepancies should be investigated to check that there have been no inadvertent mix-ups, incorrect issue and/or misappropriation of pharmaceutical products.

8. **Vehicles and equipment**

8.1 Vehicles and equipment used to distribute, store or handle pharmaceutical products should be suitable for their use and appropriately equipped to prevent exposure of the products to conditions that could affect their stability and packaging integrity, and prevent contamination of any kind.
8.2 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 pharmaceutical products being distributed.

8.3 Dedicated vehicles and equipment should be used, where possible, when handling pharmaceutical products.

8.4 Where non-dedicated vehicles and equipment are used, procedures must be in place to ensure that the quality of the pharmaceutical product will not be compromised. Appropriate cleaning should be performed, checked and recorded.

8.5 Defective vehicles and equipment should not be used, and should either be labelled as such or removed from service.

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

8.7 Vehicles, containers and equipment should be kept clean and dry and free from accumulated waste. A written cleaning programme should be available, indicating the frequency of cleaning and the methods to be used.

8.8 Vehicles, containers and equipment should be kept free from rodents, vermin, birds and other pests. There should also be written programmes for such pest control. Cleaning and fumigation agents should not have an adverse effect on product quality.
8.9 Equipment used for the cleaning of vehicles should be chosen and used so as not to constitute a source of contamination.
8.10 Special attention should be given to the design, use, cleaning and maintenance of all equipment used for the handling of pharmaceutical products which are not in a protective shipping carton or case.
8.11 Where special storage conditions (e.g. temperature and/or relative humidity), different from, or limiting, the expected environmental conditions, are required during transit these should be provided, checked, monitored and recorded. All monitoring records should be kept for a minimum of the shelflife of the product distributed plus one year, or as required by national legislation. Recorded monitoring data should be reviewed on receipt of pharmaceutical products to assess whether the required storage conditions have been met.

8.12 Equipment used for monitoring conditions within vehicles and containers, e.g. temperature and humidity, should be calibrated.

8.13 Vehicles and containers should be of sufficient capacity to allow orderly storage of the various categories of pharmaceutical products during transportation.

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

8.15 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.

9. **Shipment containers and container labelling**

9.1 All pharmaceutical products should be stored and distributed in shipment containers which do not have an adverse effect on the quality of the products, and which offer adequate protection from external influences, including contamination.

9.2 Shipping containers may not need to bear labels with full description of the identity of the container's content (in order to deter thieves), but should nonetheless provide sufficient information on handling and storage conditions and precautions to ensure the product is properly handled at all times.

9.3 The need for any special transport and/or storage conditions should be stated on the label. If a pharmaceutical product is intended for transfer outside the control of the manufacturer's products management system, the name and address of the manufacturer, special transport conditions and any special legal requirements including safety symbols should also be included on the label.
9.4 Only internationally and/or nationally accepted abbreviations, names or codes should be used in the labelling of containers.
9.5 Special care should be used when using dry ice in containers. In addition to safety issues it must be ensured that the pharmaceutical product does not come into contact with the dry ice, as it may have an adverse effect on the quality of the product.

9.6 Written procedures should be available for the handling of damaged and/or broken containers. Particular attention should be paid to those containing potentially toxic and hazardous products.

10. **Dispatch**

10.1 Pharmaceutical products should only be sold and/or distributed to persons or entities who are entitled to acquire such products as demonstrated by the applicable national, regional and international legislation. Written proof of such authority must be obtained prior to the dispatch of products to such persons or entities.

10.2 The supplier of pharmaceutical products should, prior to the dispatch of such products, ensure that the person or entity, e.g. the contract acceptor for transportation of the pharmaceutical products, is aware of and complies with the appropriate storage and transport conditions.

10.3 The dispatch and transportation of pharmaceutical products should be commenced only after the receipt of a valid delivery order or material replenishment plan which should be documented.

10.4 Written procedures for the dispatch of pharmaceutical products should be established. Such procedures should take into account the nature of the product, as well as any special precautions to be observed.

10.5 Records for the dispatch of pharmaceutical products should be prepared and should include at least the following information:
— date of dispatch;
— name and address of the entity responsible for the transportation;
— name, address and status of the addressee (e.g. retail pharmacy, hospital, 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;
— assigned batch number and expiry date;
— applicable transport and storage conditions; and
— a unique number to allow identification of the delivery order.

10.6 Records of dispatch should contain enough information to enable traceability of the pharmaceutical product. Such records should facilitate the recall of a batch of a product if necessary. Each party involved in the distribution chain has a responsibility to ensure traceability.

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

10.8 Delivery schedules should be established and routes planned, taking local needs and conditions into account. Such schedules and plans should be realistic and systematic. Care should be taken to ensure that the volume of pharmaceutical products ordered does not exceed the capacity of storage facilities at the destination.

10.9 Vehicles and containers should be loaded carefully and systematically, where applicable on a fi rst-out/last-in basis, to save time when unloading and to prevent physical damage. Extra care should be taken during loading and unloading of cartons to avoid breakage.

10.10 Pharmaceutical products should not be supplied or received after their expiry date, or so close to the expiry date that this date is likely to occur before the products are used by the consumer.

11. **Transportation and products in transit**

11.1 The transportation process should not compromise the integrity and quality of pharmaceutical products.
11.2 The manufacturer should communicate all relevant conditions for storage and transportation to those responsible for the transportation of pharmaceutical products. Such an entity(-ies) should ensure adherence to these requirements throughout transportation and at any intermediate storage stages.
11.3 Pharmaceutical products should be stored and transported in accordance with procedures such that:
• the identity of the product is not lost;
• the product does not contaminate and is not contaminated by other products;

• adequate precautions are taken against spillage, breakage, misappropriation and theft; and
• appropriate temperature and relative humidity conditions are maintained in the case of pharmaceutical products, e.g. using cold chain for thermolabile products.

11.4 A batch tracking system should be used to enable specifi c batches to be traced during the distribution process.

11.5 The required storage conditions for pharmaceutical products should be maintained within acceptable limits during transportation. There should be no gross deviation from the specifi c storage conditions for the product, or deviation for an unacceptable period of time, during the transit period. Any deviations from storage conditions which are considered to be acceptable should be determined in consultation with the marketing authorization holder and/or the manufacturer.

11.6 Where special conditions are required during transportation which are different from or limit the given environmental conditions (e.g. temperature, humidity) these should be provided, monitored and recorded.

11.7 Written procedures should be in place for investigating and dealing with any violations of storage requirements, e.g. temperature violations.

11.8 Products comprising highly active and radioactive materials, other dangerous medicines and substances presenting special risks of abuse, fi re or explosion (e.g. combustible liquids, solids and pressurized gases) should be stored in safe, dedicated and secure areas, and transported in safe, dedicated and secure containers and vehicles. In addition, applicable international agreements and national legislation should be complied with.

11.9 Products containing narcotics and other dependence-producing substances should be stored in safe and secure areas, and transported in safe and secure containers and vehicles. In addition, applicable international agreements and national legislation should be complied with.

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

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

11.12 Products containing toxic and/or flammable substances should be stored and transported in suitably designed, separate and closed containers, in accordance with national legislation and international agreements.
11.13 The interiors of vehicles and containers should remain clean and dry while pharmaceutical products are in transit.
11.14 Packaging materials and transportation containers should be of suitable design to prevent damage of pharmaceutical products during transport.
11.15 Sufficient security should be provided to prevent theft and other misappropriation of products. Steps should be taken to prevent unauthorized access to pharmaceutical products during transport.
11.16 Damage to containers and any other event or problem which occurs during transit must be recorded and reported to the relevant department, entity or authority, and investigated.

11.17 Pharmaceutical products in transit must be accompanied by the appropriate documentation.

12. **Documentation**

12.1 Written instructions and records should be available which document all activities relating to the distribution of pharmaceutical products, including all applicable receipts and issues. The name of the applicable entity should appear on all relevant documents.

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

12.3 Documents, and in particular instructions and procedures relating to any activity that could have an impact on the quality of pharmaceutical products, should be designed, completed, reviewed and distributed with care.

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

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

12.6 The nature, content and retention of documentation relating to the distribution of pharmaceutical products should comply with national legislative requirements. Where such requirements are not in place the docu-

ments should be retained for a period equal to the shelf-life of the products where applicable, plus one year.

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

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

12.9 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.

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

12.11 Records relating to storage of pharmaceutical products should be kept and be readily available upon request in accordance with the WHO guidelines on good storage practice (*1*).
12.12 Permanent records, written or electronic, should exist for each stored product indicating recommended storage conditions, any precautions to be observed and retest dates. Pharmacopoeial requirements and current national regulations concerning labels and containers should be respected at all times.
12.13 Procedures should be in place for temperature mapping, security services to prevent theft or tampering with goods at the storage facilities, destruction of unsaleable stocks and on retention of the records.
12.14 In the case of temperature-sensitive pharmaceutical products, records of investigations and actions should be retained for at least one year after the expiry date of the product.
12.15 Where the records are generated and kept in electronic form, backups should be maintained to prevent any accidental data loss.

13. **Repackaging and relabelling**

13.1 Repackaging (including relabelling) of pharmaceutical products should only be performed by distributors appropriately authorized and/or licensed to do so, and in accordance with GMP principles. Where these functions are performed they should comply with the applicable national, regional and international guidelines relating to repackaging and relabelling of pharmaceutical products.

14. **Complaints**

14.1 There should be a written procedure in place for the handling of complaints. A distinction should be made between complaints about a product or its packaging and those relating to distribution. In the case of a complaint about the quality of a product or its packaging the original manufacturer and/or marketing authorization holder should be informed as soon as possible.
14.2 All complaints and other information concerning potentially defective and potentially counterfeit pharmaceutical products should be reviewed carefully according to written procedures describing the action to be taken, including the need to consider a recall where appropriate.

14.3 Any complaint concerning a material defect should be recorded and thoroughly investigated to identify the origin or reason for the complaint (e.g. repackaging procedure or original manufacturing process).

14.4 If a defect relating to a pharmaceutical product is discovered or suspected, consideration should be given to whether other batches of the product should also be checked.

14.5 Where necessary, appropriate follow-up action should be taken after investigation and evaluation of the complaint.

15. **Recalls**

15.1 There should be a system which includes a written procedure, to recall promptly and effectively pharmaceutical products known or suspected to be defective, with a designated person(s) responsible for recalls.

15.2 Such procedures should be checked regularly and updated as necessary.
15.3 The original manufacturer and/or marketing authorization holder should be informed in the event of a recall. Where a recall is instituted by an entity other than the original manufacturer and/or marketing authorization holder, consultation with the original manufacturer and/or marketing authorization holder should, where possible, take place before the recall is instituted.

15.4 The effectiveness of the arrangements for recalls should be evaluated at regular intervals. All recalled pharmaceutical products should be stored in a secure, segregated area pending appropriate action.

15.6 Recalled pharmaceutical products should be segregated during transit and clearly labelled as recalled products. Where segregation in transit is not possible, such goods must be securely packaged, clearly labelled, and be accompanied by appropriate documentation.

15.7 The storage conditions applicable to a pharmaceutical product which is subject to recall should be maintained during storage and transit until such time as a decision has been made regarding the fate of the product in question.
15.8 All customers and competent authorities of all countries to which a given pharmaceutical product may have been distributed should be informed promptly of any intention to recall the product because it is, or is suspected to be, defective.
15.9 All records should be readily available to the designated person(s) responsible for recalls. These records should contain sufficient information on pharmaceutical products supplied to customers (including exported products).

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

16. **Rejected and returned products**

16.1 Rejected pharmaceutical products and those returned to a distributor should be appropriately identified and handled in accordance with a procedure which involves at least the physical segregation of such pharmaceutical products in quarantine in a dedicated area, or other equivalent (e.g. electronic) segregation, to avoid confusion and prevent distribution until a decision has been taken with regard to their disposition. The storage conditions applicable to a pharmaceutical product which is rejected or returned should be maintained during storage and transit until such time as a decision has been made regarding the product in question.

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

16.3 Provision should be made for the appropriate and safe transport of returned products in accordance with the relevant storage and other requirements.

16.4 Provision should be made for the appropriate and safe transport of rejected and waste materials prior to their disposal.

16.5 When pharmaceutical products are destroyed this should be done in accordance with international, national and local requirements regarding

disposal of such products, and with due consideration to protection of the environment.
16.6 Records of all returned, rejected and/or destroyed pharmaceutical products should be kept.

17. **Counterfeit pharmaceutical products** 

17.1 Any counterfeit or suspected counterfeit medicines found in the pharmaceutical supply chain should be segregated immediately from other pharmaceutical products and recorded.
17.2 The holder of the marketing authorization, the appropriate national and/or international regulatory bodies, as well as other relevant competent authorities, should be informed immediately.
17.3 Such products should be clearly labelled to prevent further distribution or sale.
17.4 Upon confirmation of the product being counterfeit a formal decision should be taken on its disposal and the decision recorded.

18. **Importation**

18.1 Consideration should be given to the WHO guidelines on import procedures for pharmaceutical products (*5*). The following aspects should be given particular attention.

18.2 The number of ports of entry in a country for the handling of imports of pharmaceutical products should be limited by appropriate legislation.

18.3 The most appropriately located and best equipped to handle imports of pharmaceutical products should be chosen as the port(s) of entry for the import of such products into a country.

18.4 At the port of entry, consignments of pharmaceutical products should be stored under suitable conditions for as short a time as possible.

18.5 All reasonable steps should be taken by importers to ensure that products are not mishandled or exposed to adverse storage conditions at wharves or airports.

18.6 Where necessary, people with pharmaceutical training should be involved with the customs procedures or should be readily contactable.

18.7 The WHO Certification Scheme on the quality of pharmaceutical products moving in international commerce should be used to provide data regarding quality assessment of imported pharmaceutical products.

19. **Contract activities**

19.1 Any activity relating to the distribution of a pharmaceutical product which is delegated to another person or entity should be performed according to the terms of a written contract which is agreed upon by the contract giver and the contract accepter.
19.2 The contract should defi ne the responsibilities of each party including observance of the principles of GDP.
19.3 All contract accepters should comply with the requirements in these guidelines.
19.4 Subcontracting may be permissible under certain conditions subject to the written approval of the contract giver.
19.5 Any contract accepter should be audited periodically.

20. **Self-inspection**

20.1 The system of quality assurance should include self-inspections. These should be conducted to monitor implementation and compliance with the principles of GDP and if necessary, to trigger corrective and preventive measures.
20.2 Self-inspections should be conducted in an independent and detailed way by a designated, competent person.
20.3 The results of all self-inspections should be recorded. Reports should contain all observations made during the inspection and, where applicable, proposals for corrective measures. There should be an effective follow-up programme. Management should evaluate the inspection report, and the records of any corrective actions taken.
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ANNEX B

WHO Technical Report Series, No. 908, 2003

Annex 9
Guide to good storage practices for pharmaceuticals[1]

1. Introduction

This guide is intended for those involved in the storage, transportation and distribution of pharmaceuticals. It is closely linked to other existing guides recommended by the WHO Expert Committee on Specifications for Pharmaceutical Preparations, such as:

- Good trade and distribution practice (GTDP) of pharmaceutical starting materials (*1*);
- The stability testing of pharmaceutical products containing well-established drug substances in conventional dosage forms (information given in connection with regulation for marketing authorization) (*2*);
- Good manufacturing practices (GMP) (*3*);

[1] This guidance has been prepared in close collaboration with the International Pharmaceutical Federation (FIP).

- The cold chain, especially for vaccines and biologicals;
- *The International Pharmacopoeia* (*4*).

The objective of this guide is to supplement the above-mentioned documents by describing the special measures considered appropriate for the storage and transportation of pharmaceuticals. However, they may be adapted to meet individual needs where necessary, provided that the desired standards of quality are still achieved.

The guidelines are applicable not only to manufacturers of medicinal products but also to pharmaceutical importers, contractors and wholesalers, and community and hospital pharmacies. They should be adjusted in line with the type of activity where the storage of pharmaceuticals is taking place. National or regional regulations should be followed for all related activities.

2. Glossary

The definitions given below of some of the terms used in this document take into account the terminology of current regulations and recommendations.

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.

contamination
The undesired introduction of impurities of a chemical or microbiological nature, or of foreign matter, into or onto a starting material, or intermediate or finished product during production, sampling, packaging or repackaging, storage or transport.

cross-contamination
Contamination of a starting material, intermediate product or finished product with another starting material or product during production.

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 drug product up to and including 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.

labelling
The action involving the selection of the correct label, with the required information, followed by line clearance and application of the label.

manufacture
All operations of purchase of materials and products, production, quality control, release, storage and distribution of finished products, and the related controls.

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.

pharmaceutical product
Any medicine intended for human use or veterinary product administered to food-producing animals, presented in its finished dosage form or as a starting material for use in such a dosage form, that is subject to control by pharmaceutical legislation in both the exporting state and the importing state.

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.

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

storage
The storing of pharmaceutical products and materials up to their point of use.

supplier
A person providing pharmaceutical products and materials on request. Suppliers may be agents, brokers, distributors, manufacturers or traders. Where possible, suppliers should be authorized by a competent authority.

3. Personnel

3.1 At each storage site (e.g. that of a manufacturer, distributor, wholesaler, community or hospital pharmacy) there should be an adequate number of qualified personnel to achieve pharmaceutical quality assurance objectives. National regulations on qualifications should be followed.

3.2 All personnel should receive proper training in relation to good storage practice, regulations, procedures and safety.

3.3 All members of staff should be trained in, and observe high levels of, personal hygiene and sanitation.

3.4 Personnel employed in storage areas should wear suitable protective or working garments appropriate for the activities they perform.

4. Premises and facilities

Storage areas

4.1 Precautions must be taken to prevent unauthorized persons from entering storage areas.

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

4.3 Storage areas should be designed or adapted to ensure good storage conditions. In particular, they should be clean and dry and maintained within acceptable temperature limits. Where special storage conditions are required on the label (e.g. temperature, relative humidity), these should be provided, checked, monitored and recorded. Materials and pharmaceutical products should be stored off the floor and suitably spaced to permit cleaning and inspection. Pallets should be kept in a good state of cleanliness and repair.

4.4 Storage areas should be clean, and free from accumulated waste and vermin. 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. There should also 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 pharmaceutical products. There should be appropriate procedures for the clean up of any spillage to ensure complete removal of any risk of contamination.

4.5 Receiving and dispatch bays should protect materials and products from the weather. Reception areas should be designed and equipped to allow containers of incoming materials and pharmaceutical products to be cleaned, if necessary, before storage.

4.6 Where quarantine 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 quarantine should provide equivalent security. For example, computerized systems can be used, provided that they are validated to demonstrate security of access.

4.7 There should normally be a separate sampling area for starting materials in a controlled environment. If sampling is performed in the storage area, it should be conducted in such a way as to prevent contamination or cross-contamination. Adequate cleaning procedures should be in place for the sampling areas.

4.8 Physical or other equivalent validated (e.g. electronic) segregation should be provided for the storage of rejected, expired, recalled or returned materials or products. The materials or products, and areas concerned should be appropriately identified.

4.9 Highly active and radioactive materials, narcotics and other hazardous, sensitive and/or dangerous materials and pharmaceutical 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.

4.10 Materials and pharmaceutical products should be handled and distributed according to GMP as defined in this document.

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

4.12 Materials and pharmaceutical 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.

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

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

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

4.16 Storage areas should provide adequate lighting to enable all operations to be carried out accurately and safely.

Storage conditions

4.17 Storage conditions for pharmaceutical products and materials should be in compliance with the labelling, which is based on the results of stability testing (see Appendix).

Monitoring of storage conditions

4.18 Recorded temperature monitoring data should be available for review. The equipment used for monitoring should be checked at suitable predetermined intervals and the results of such checks should be recorded and retained. All monitoring records should be kept for at least the shelf-life of the stored material or product plus 1 year, or as required by national legislation. Temperature mapping should show uniformity of the temperature across the storage facility. It is recommended that temperature monitors be located in areas that are most likely to show fluctuations.

4.19 Equipment used for monitoring should also be calibrated at defined intervals.

5. Storage requirements

Documentation: written instructions and records

5.1 Written instructions and records should be available which document all activities in the storage areas including the handling of expired stock. These should adequately describe the storage procedures and define the route of materials and pharmaceutical products and information through the organization in the event of a product recall being required.

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

5.3 Records should be kept for each delivery. They should include the description of the goods, quality, quantity, supplier, supplier's batch number, the date of receipt, assigned batch number and the expiry date. Where national regulations prescribe that records must be retained for a certain period, this must be observed. (Otherwise such records should be retained for a period equal to the shelf-life of the incoming materials and products, where applicable, plus 1 year).

5.4 Comprehensive records should be maintained showing all receipts and issues of materials and pharmaceutical products according to a specified system, e.g. by batch number.

Labelling and containers

5.5 All materials and pharmaceutical products should be stored in containers which do not adversely affect the quality of the materials or products concerned, and which offer adequate protection from external influences. In some circumstances, this could include bacterial contamination.

5.6 All containers should be clearly labelled with at least the name of the material, the batch number, the expiry date or retest date, the specified storage conditions and reference to the pharmacopoeia, where applicable. Unauthorized abbreviations, names or codes should not be used.

Receipt of incoming materials and pharmaceutical products

5.7 On receipt, each incoming delivery should be checked against the relevant purchase order and each container physically verified, e.g. by the label description, batch number, type of material or pharmaceutical product and quantity.

5.8 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.

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

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

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

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

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

Stock rotation and control

5.14 Periodic stock reconciliation should be performed by comparing the actual and recorded stocks.

5.15 All significant stock discrepancies should be investigated as a check against inadvertent mix-ups and/or incorrect issue.

5.16 In manufacturing facilities, partly used containers of materials and pharmaceutical products should be securely reclosed and resealed to prevent spoilage and/or contamination during subsequent storage. Materials and pharmaceutical products from containers which have been opened or partly used should be used up before those in unopened containers.

5.17 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 control. Any action taken should be documented.

Control of obsolete and outdated materials and pharmaceutical products

5.18 All stocks should be checked regularly for obsolete and outdated materials and pharmaceutical products. All due precautions should be observed to prevent the issue of outdated materials and pharmaceutical products.

6. Returned goods

6.1 Returned goods, including recalled goods, should be handled in accordance with approved procedures and records should be maintained.

6.2 All returned goods should be placed in quarantine and returned to saleable stock only after this has been approved by a nominated, responsible person following a satisfactory quality re-evaluation.

6.3 Any stock reissued should be so identified and recorded in stock records. Pharmaceuticals returned from patients to the pharmacy should not be taken back as stock, but should be destroyed.

7. Dispatch and transport

7.1 Materials and pharmaceutical products should be transported in such a way that their integrity is not impaired and that storage conditions are maintained.

7.2 Special care should be exercised when using dry ice in cold chains. In addition observing to safety precautions, it must be ensured that the materials or product does not come in into contact with dry ice, as this may adversely affect the product quality, e.g. by freezing.

7.3 Where appropriate, the use of devices to monitor conditions such as temperature during transportation is recommended. Monitoring records should be available for review.

7.4 The dispatch and transport of materials and pharmaceutical products should be carried out only after receipt of a delivery order. The receipt of the delivery order and the dispatch of the goods must be documented.

7.5 Dispatch procedures should be established and documented, taking into account the nature of the materials and pharmaceutical products concerned and any special precautions that might be required.

7.6 The outside container should offer adequate protection from all external influences and should be indelibly and clearly labelled.

7.7 Records for dispatch should be retained, stating at least:

— the date of dispatch;
— the customer's name and address;
— the product description, e.g. name, dosage form and strength (if appropriate), batch number and quantify;
— the transport and storage conditions.

7.8 All records should be readily accessible and available on request.

8. Product recall

8.1 There should be a procedure to recall from the market, promptly and effectively, pharmaceutical products and materials known or suspected to be defective.

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Appendix

Storage and labelling conditions[2]

Normal storage conditions

Storage in dry, well-ventilated premises at temperatures of 15–25 °C or, depending on climatic conditions, up to 30 °C. Extraneous odours, other indications of contamination, and intense light must be excluded.

Defined storage instructions

Drug products that must be stored under defined conditions require appropriate storage instructions. Unless otherwise specifically stated (e.g. continuous maintenance of cold storage) deviation may be tolerated only during short-term interruptions, for example, during local transportation.

The use of the following labelling instructions are recommended:

On the label	*Means*
"Do not store over 30 °C"	from +2 °C to +30 °C
"Do not store over 25 °C"	from +2 °C to +25 °C
"Do not store over 15 °C"	from +2 °C to +15 °C
"Do not store over 8 °C"	from +2 °C to +8 °C
"Do not store below 8 °C"	from +8 °C to +25 °C
"Protect from moisture"	no more than 60% relative humidity in normal storage conditions; to be provided to the patient in a moisture-resistant container.
"Protect from light"	to be provided to the patient in a light-resistant container.

[2] The text was adopted by the WHO Expert Committee on Specifications for Pharmaceutical Preparations at its 34th meeting (*WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-Fourth report.* Geneva, World Health Organization, 1996, Annex 5 (WHO Technical Report Series No. 863).