ETHIOPIAN FOOD AND DRUG AUTHORITY

GUIDELINES FOR:

GOOD STORAGE PRACTICES

GOOD DISTRIBUTION PRACTICE

PHARMACEUTICAL PRODUCT RECALL

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Signature

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Acronyms

API	Active Pharmaceutical Ingredient
CAPA	Corrective Action and Preventive Action
EFDA	Ethiopian Food and Drug Authority
GDP	Good Distribution Practices
GMP	Good Manufacturing Practices
GPP	Good Pharmacy Practices
GSP	Good Storage Practices
GTDP	Good Trade and Distribution Practices
ICH	The International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)
PQM	Promoting the Quality of Medicines Program
SFPP	Substandard and falsified pharmaceutical products
SOP	Standard Operating Procedure
USAID	United States Agency for International Development
USP	U. S. Pharmacopeial Convention
WHO	World Health Organization

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Definitions

The definitions given below should be used in the context of this guideline only.

Agreement: An 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 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 its labels, its batch records and corresponding certificates of analysis.

Consignment: The quantity of pharmaceutical products supplied at one time in response to a particular request or order. A consignment may comprise 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. Transportation containers are container which is used during transportation of the pharmaceutical products.

Contamination: The undesired introduction of impurities of a chemical or microbiological nature or of foreign matter, into or onto 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; this may include quality elements in the agreement, or in a separate contract.

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 or medical product with another starting material or product, during production, storage and transportation.

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

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

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

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 or 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 national regulatory authority (NRA).

"Source" shall refer to the identification, including name and address, of the marketing authorization holder, manufacturer, importer, exporter, distributor or retailer, as applicable

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.

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). The group of good practice guides governing the preclinical, clinical, manufacture, testing, storage, distribution and post-market activities for regulated medical products, such as good laboratory practices (GLP), good clinical practices (GCP), good

manufacturing practices (GMP), good pharmacy practice (GPP), good distribution practices (GDP) and other good practices.

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 their storage.

Heating, ventilation and air conditioning systems. Heating, ventilation and air conditioning, also referred to as environmental control systems.

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.

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

Intermediate product: A partly processed product that must undergo further manufacturing steps before it becomes a bulk finished product.

Labeling: The 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; and names and addresses of the manufacturer and/or the supplier.

Licensee: The person or business with the primary responsibility for the product supply; the Licensee could be the manufacturer, importer, marketing authorization holder, wholesaler or any other institutions licensed to hold/import/distribute pharmaceutical products.

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

Marketing authorization: A legal document issued by the competent medicine's 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 INNs), the shelf-life and storage conditions, and packaging characteristics.

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 including in vitro diagnostic medical devices, and vaccines.

Packaging Materia: Any material, including printed material, employed in the packaging of a medical 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 transactions relating to a pharmaceutical product as it is distributed through the supply chain.

Pharmaceutical product: Any product intended for human use, presented in its finished dosage form, which is subject to control by pharmaceutical legislation in either the exporting or the importing state and includes products for which a prescription is required, products that may be sold to patients without a prescription, biologicals and vaccines.

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 and substandard. The recall might be initiated by the manufacturer, importer, wholesaler, distributor or a responsible agency.

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 medical products in the supply chain.

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.

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.

Self-inspection: An internal procedure followed to evaluate the entity's compliance with GSP and GDP, as well as 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 NRAs but fail to meet either national or international quality standards or specifications – or, in some cases, both.

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 product

PART-I: Pharmaceutical Quality Assurance Guide for good storage and distribution practices.

1. Introduction

The principles of GSDP are applicable both to pharmaceutical products moving forward in the storage and distribution chain from the manufacturer to the entity responsible for dispensing or providing medicinal products to the patient and to the products that are moving backward in the supply chain, for example, as a result of the return or recall thereof. All entities involved in the storage distribution processes should apply due diligence with adherence to the principles of GSDP.

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

Storage and distributors organization should maintain a quality system setting out responsibilities, processes, risk management principles, self-inspection, complaint handling in relation to their activities.

2. Quality management

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

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

3. Within an organization, quality assurance serves as a management tool. There should be a documented quality policy describing the overall intentions and requirements of the distributor regarding quality, as formally expressed and authorized by management.

4. The quality system should include an appropriate organizational structure, procedure, processes and resources and systematic actions necessary to ensure adequate confidence that a product or service and its documentation will satisfy given requirements for quality. The totality of these actions is described as the quality system.

5. Duties and responsibilities should be clearly defined and understood by the individuals concerned and recorded as written job descriptions. At every level of the supply chain, employees should be fully informed and trained in their duties and responsibilities.

6. A designated person should be appointed within the organization, who has defined authority and responsibility for ensuring that a quality system is implemented and maintained.

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

8. The quality system should foster a safe, transparent and secure distribution system that includes product traceability throughout the supply chain. There should be procedures in place to ensure document traceability of products received and distributed to facilitate product recall.

9. All parties involved in the pharmaceutical supply chain should be identifiable.

10. Measures should be in place to ensure that pharmaceutical products have documentation that can be used to permit traceability of the products throughout distribution channels from the manufacturer/importer to the entity responsible for selling or supplying the product to the patient or his or her agent.

11. Records including expiry dates and batch numbers should be part of a secure distribution documentation enabling traceability.

12. There should be a procedure in place for the creation and maintenance of a pedigree for pharmaceutical products. Provision should be made for a visual and/or analytical identification

of potential SFPP. The procedure to be followed when a suspected product is identified should include provisions for notification, as appropriate, of the holder of the marketing authorization, entity identified on the label (if different from the manufacturer), the appropriate national and/or international regulatory bodies, as well as other relevant competent authorities.

13. The quality system should ensure that:

    — GSP and GDP are adopted and implemented to ensure that that quality of medical products is maintained throughout their shelf life in the supply chain; and medical products are appropriately procured, stored, distributed and delivered (in compliance with the legislation) to the appropriate recipients

    — 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.

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

    — there are systems to manage changes, deviations and corrective and

    — preventive actions (CAPAs).

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

15. 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.

16. Roles and responsibilities should be clearly defined and understood by the individuals concerned and recorded as written job descriptions.

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

3. Substandard and falsified pharmaceutical products

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

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.

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

4. Records should be maintained reflecting the investigations and action taken, such as disposal of the product. Falsified products should not reenter the market.

4. Self-inspection

1. Self-inspection monitors the implementations and compliance with the principles of GSDP. Self-inspections should be conducted in order to monitor implementation and compliance with these

2. Self-inspections should be conducted by a competent designated person

3. Self-inspections should be recorded; reports should contain observations and corrective actions taken and recorded.

4. The quality system should include self-inspections. These should be conducted to monitor implementation and compliance with the principles of GSP/GDP and, if necessary, to trigger corrective and preventive measures.

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

6. 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.

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

8. The team conducting the inspection should be free from bias and individual members should have appropriate knowledge and experience.

9. Necessary CAPAs should be taken, and their effectiveness should be reviewed within a defined timeframe.

5. Quality risk management

1. There should be a system to assess, control, communicate and review risks identified at all stages in the supply chain.
2. The evaluation of risk should be based on scientific knowledge and experience and ultimately be linked to the protection of the patient.
3. Organizations from time to time, should conduct risk assessments to assess potential risks to the quality and integrity of pharmaceutical products. The quality system should be developed and implemented to address any potential risks identified.
4. Appropriate controls should be developed and implemented to address all risks. The effectiveness of the controls implemented should be evaluated at periodic intervals.

5. The quality system should be reviewed and revised periodically to address new risks identified during a risk assessment.

6. Management review

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

2. 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.

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

7. Complaints

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.
2. All complaints and other information concerning potentially defective and potentially SF pharmaceutical products should be reviewed carefully according to written procedures describing the action to be taken, including the need to consider a recall where

appropriate. Consideration should be given to whether other batches of the product should also be checked.

3. 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.
4. Where required, the information should be shared to EFDA, and a recall initiated where appropriate.
5. A distinction should be made between complaints about a medical product or its packaging and those relating to distribution.
6. The relevant information, such as the results of the investigation of the complaint, should be shared with the relevant entities.
7. Pharmaceutical 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.
8. Appropriate follow-up action should be taken after investigation and evaluation of the complaint. There should be a system in place to ensure that the complaint, the response received from the original product manufacturer, or the results of the investigation of the complaint, are shared with all the relevant parties.

8. Recalls

1. There should be a system, which includes a written procedure, to effectively and promptly recall pharmaceutical products known or suspected to be defective or Substandard and falsified pharmaceutical products, with a designated person(s) responsible for recalls. The system should comply with the guidance issued by the national or regional regulatory authority. This procedure should be checked regularly and updated as necessary.
2. The original manufacturer and/or marketing authorization holder should be informed in the event of a recall. Where a recall is instituted by an entity other than the original

manufacturer and/or marketing authorization holder, consultation with the original manufacturer and/or marketing authorization holder should, where possible, take place before the recall is instituted. Information on a recall should be shared with the appropriate national or regional regulatory authority. If a recall of the original product is necessary because of a Substandard and falsified pharmaceutical product which is not easily distinguishable from the original product, the manufacturer of the original product and the relevant health authority should be informed.

3. 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.
4. Recalled pharmaceutical products should be segregated during transit and clearly labeled as recalled products. Where segregation in transit is not possible, such goods must be securely packaged, clearly labeled, and be accompanied by appropriate documentation.
5. The particular storage conditions applicable to a pharmaceutical product which is subject to recall should be maintained during storage and transit until such time as a decision has been made regarding the fate of the product in question.
6. All customers and competent authorities of all countries to which a given pharmaceutical product may have been distributed should be informed promptly of any intention to recall the product because it is, or is suspected to be, defective or Substandard and falsified pharmaceutical products.
7. All records should be readily available to the designated person(s) responsible for recalls. These records should contain sufficient information on the pharmaceutical products supplied to customers (including exported products).
8. The progress of a recall process should be recorded, and a final report issued, which includes reconciliation between the amount delivered and the quantities of concerned products/batches.

9. Documentation

1. Written instructions and records that document all activities relating to the distribution of pharmaceutical products, including all applicable receipts and issues (invoices), should be made available. Records should be kept for expiry date plus one year.
2. Distributors should keep records of all pharmaceutical products received. Records should contain at least the following information:
   —Date;
   —Name of the pharmaceutical product;
   —Batch number;
   —Expiry date;
   —Name and address of the client;
   —Quantity received, or supplied; and
   —Name and address of the supplier.

3. Procedures should be established and maintained for the preparation, review, approval, use of and control of changes to all documents relating to the distribution process. Procedures must be in place for both internally generated documents and those from external sources.
4. 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.
5. 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.
6. 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.
7. The nature, content and retention of documentation relating to the distribution of pharmaceutical products and any investigations conducted and actions taken, should comply

with national legislative requirements. Where such requirements are not in place, the documents should be retained for at least one year after the expiry date of the product concerned.

8. The distributor must establish and maintain procedures for the identification, collection, indexing, retrieval, storage, maintenance, disposal of and access to all applicable documentation.
9. All records must be readily retrievable and must be stored and retained using facilities that are safeguarded against unauthorized modification, damage, deterioration and/or loss of documentation. 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.
10. Mechanisms should exist to allow for the 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.
11. Records relating to storage of pharmaceutical products should be kept and be readily available upon request in accordance with the EFDA Guidelines on Good Storage Practices for Pharmaceuticals
12. Permanent records, written or electronic, should exist for each stored product indicating recommended storage conditions, any precautions to be observed and retest dates. Pharmacopeial requirements and current national regulations concerning labels and containers should be respected at all times.
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 or unusable stocks and retention of the records.
14. Where the records are generated and kept in electronic form, backups should be maintained to prevent any accidental data loss.

10. Outsourced activities

1. Any activity relating to the storage and distribution of a medical product that is delegated to another person or entity should be performed by the appropriately authorized parties, in accordance with national legislation and the terms of a written contract.
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;
   - the 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.
3. The contract giver should assess the contract acceptor before entering into the contract, e.g. through on-site audits, documentation and licensing status review.
4. The contract giver should provide to the contract acceptor all relevant information relating to the material and medical products.
5. The contract acceptor should have adequate resources (e.g. premises, equipment, personnel, knowledge, experience and vehicles, as appropriate) to carry out the work.
6. The contract acceptor should refrain from performing any activity that may adversely affect the materials or products handled.

11. Inspection of storage and distribution facilities

1. Storage and distribution facilities should be inspected by inspectors authorized by national legislation. This should be done at determined, periodic intervals.
2. Inspectors should have appropriate educational qualifications, knowledge and experience.
3. An inspection should normally be conducted by a team of inspectors.
4. Inspectors should assess compliance with national legislation, GSP, GDP, as appropriate.

5. Inspections should cover the premises, equipment, personnel, activities quality system, qualification and validation, calibration and other related aspects, as contained in this guideline.
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.
7. Observations may be categorized based on risk assessment.
8. CAPA for observations listed as non-compliances in the inspection report, should be submitted for review by the inspectors within the defined period, as stated by the inspectors.
9. Inspections should be closed with a conclusion after the review of the CAPAs.

PART-II: Guidelines for Good Storage Practices

1. Introduction

EFDA has prepared these guidelines because the quality and integrity of pharmaceutical products and materials can be affected with lack of control during storage and poor compliance to good storage practices.

This guide is intended for those involved in the storage, transportation and distribution of pharmaceuticals. It is closely linked to other existing guidelines of the Ethiopian Food and Drug Authority (EFDA) and other recognized guidelines of the World Health Organization (WHO) or The International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).

2. Objective

The objective of this guide is to describe the minimum requirements considered appropriate for the storage and transportation of pharmaceuticals products and materials so that to avoid safety, efficacy and quality problems caused by improper storage practice of pharmaceutical products and materials.

3. Scope

These guidelines are applicable not only to manufacturers of medicinal products, but also to pharmaceutical importers, wholesalers, medicine retail outlets and hospital pharmacies as well as other facilities which stores medicines. They should be adjusted in line with the type of activity where the storage of pharmaceuticals is taking place.

4. Personnel

1. There should be an adequate number of personnel.
2. Personnel should have appropriate educational qualification, experience and training relative to the activities undertaken.
3. A designated person within the organization, with appropriate qualification and training, should have the defined authority and responsibility for ensuring that a quality management system is implemented and maintained.
4. This person should preferably be independent from the person responsible for operations and should ensure compliance with GSP and GDP.
5. 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.
6. There should be arrangements in place to ensure that management and personnel are not subjected to commercial, political, financial or 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.
7. Safety procedures should be in place relating to all relevant personnel and property, environmental protection and product integrity.

8. Personnel should receive initial and continued training in accordance with a written training programme. The training should cover the requirements of GSP and 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.

9. 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.

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

11. Records of all training, attendance and assessments should be kept.

12. 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.

13. 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.

14. 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.

15. Codes of practice and 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 falsification of any product.

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

17. Staff should be medically examined before being employed and at regular intervals after employment. A medical check-up record should be maintained for each employee.

18. Before being employed an applicant background should be investigated. Staff with conviction of theft or drug abuse should not be employed.

19. A written job description of the responsible person should define his/her authorization to make decisions with regard to his/her responsibilities.

20. Personnel working in the storage areas should have at least basic knowledge of the following:

    — the types of material and the dosage forms to be handled
    — Materials and pharmaceutical products that require special storage conditions
    — types of storage conditions
    — types of stability (physical, chemical, microbiological, toxicological, etc.
    — expiration date.

5. Premises and facilities

Premise and other areas utilized for storage purposes should comply with the minimum standards set by EFDA. This must be located, designed, constructed, modified and maintained to suit the operation carried out and to protect from potentially harmful influences such as undue variation of temperature and humidity, dust, odor and entry of animals, vermin and insects. The floor and should be smooth and free of recess and easy to clean. There should be also adequate light and ventilation.

6. Storage areas

1. Precautions must be taken to prevent unauthorized persons from entering storage areas.
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.
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.
4. 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.
5. Storage areas should be clean, and free from accumulated waste and vermin. A written sanitation program 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 program 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 in place for the cleanup of any spillage to ensure complete removal of any risk of contamination.
6. 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.
7. 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.

8. 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.
9. 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.
10. Highly toxic 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.
11. Materials and pharmaceutical products should be handled and stored in such a manner as to prevent contamination, mix-ups and cross-contamination.
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.
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 made on their fate.
14. Narcotic drugs and other controlled materials and pharmaceutical products should be stored in compliance with international conventions, and national laws and regulations on narcotics.
15. Broken or damaged items should be withdrawn from usable stock and separated.
16. Storage areas should provide adequate lighting to enable all operations to be carried out accurately and safely.

7. Storage conditions

1. Materials and pharmaceutical products must be stored under conditions which minimize deterioration, contamination or damage. They must be stored under conditions compatible with their recommended storage requirements of temperature and /or humidity.
2. The storage conditions for pharmaceutical products should be in compliance with their labelling and information provided by the manufacturer.
3. Heating, ventilation and air conditioning systems should be appropriately designed, installed, qualified and maintained, to ensure that the required storage conditions are upheld.
4. Mapping studies for temperature, and relative humidity where appropriate, should be done, for example in storage areas, refrigerators and freezers
5. 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 its intended use.
6. All records pertaining to mapping and monitoring should be kept for a suitable period of time and as required by national legislation.

8. Monitoring of storage conditions

1. Recorded temperature and relative humidity 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 one year.
2. 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 fluctuation.

9. Storage requirements

Documentation: Written Instructions and Records

1. Documentation includes all procedures, records and data, whether in paper or electronic form.
2. Documents should be appropriately designed, completed, reviewed, authorized, distributed and kept as required.
3. Written procedures should be followed for the preparation, review, approval, use of and control of all documents relating to the policies and activities for the process of storage and distribution of medical products.
4. 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 a product recall is required.
5. 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. Pharmacopeial requirements and current national regulations concerning labels and containers should be respected at all times.
6. Records should be kept for each delivery that include the description of the goods, quality, quantity, supplier, supplier's batch number, date of receipt, assigned batch number and expiry date. Such records should be retained for a period equal to the shelf-life of the incoming materials and products, and plus one year.
7. All documents should be completed, signed and dated as required by authorized person(s) and should not be changed without the necessary authorization.
8. Documentation should be prepared and maintained in accordance with the national legislation and principles of good documentation practices
9. Records should be accurate, legible, traceable, attributable and unambiguous. Electronic data should be backed-up in accordance with written procedures. Records should be maintained for the back-up and restoration of data.
10. 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.

11. 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.
12. 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;
    - suitability of the supplier;
    - qualification of suppliers; and
    - customer qualification.

10. Container and labeling

1. 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.
2. 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.

11. Receipt of incoming materials and pharmaceutical products

1. Upon 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.
2. The consignment should be examined for uniformity of the containers and, should the delivery comprise more than one batch, should be subdivided according to the supplier's batch numbers.
3. 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.
4. 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 labeled accordingly.
5. Following sampling, the goods should be subject to quarantine. Batch segregation should be maintained during quarantine and all subsequent storage.
6. Materials and pharmaceutical products should remain in quarantine until an authorized release or rejection is obtained.
7. Measures should be taken to ensure that rejected materials products cannot be used. They should be stored separately from other materials and pharmaceutical products while awaiting destruction or return to the supplier.

12. Stock rotation and control

1. Periodic stock reconciliation should be performed by comparing the actual and recorded stocks.
2. All significant stock discrepancies should be investigated as a check against inadvertent mix-ups and/or incorrect issue.
3. 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 that have been opened or partly used should be used up before those in unopened containers.

4. Damaged containers should not be used 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 its control. Any actions taken should be documented.

13. Control of obsolete and outdated materials and pharmaceutical products

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

14. Management of returned goods

1. Returned pharmaceutical products should be handled in accordance with authorized procedures.
2. All returned medical products should be placed in quarantine upon receipt.
3. The status of the goods should be clear. Precautions should be taken to prevent access and distribution until a decision has been taken with regard to their disposition. The particular storage conditions applicable to the medical products should be maintained until their disposition.
4. 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.
5. 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.

6. 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; and

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

7. Where products are rejected, authorized procedures should be followed, including safe transport.
8. Destruction of products should be done in accordance with international, national and local requirements regarding disposal of such products, and with due consideration to the protection of the environment.
9. Records of all returned, rejected and destroyed medical products should be kept for a defined period, in accordance with national requirements.

15. Dispatch

1. The dispatch of 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.
2. 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.
3. The outside container should offer adequate protection from all external influences and should be indelibly and clearly labeled.
4. Dispatch should be undertaken only after the receipt of a valid order, which should be documented.
5. Pharmaceutical products should only be sold and/or distributed to persons or entities that are authorized to acquire such products in accordance with the applicable national and

importing country legislation. Written proof of such authority must be obtained prior to the distribution of products to such persons or entities.

6. Prior to the dispatch of the pharmaceutical products, the supplier should ensure that the person or entity, e.g., the contract acceptor for transportation of the pharmaceutical products, is aware of the pharmaceutical products to be distributed and complies with the appropriate storage and transport conditions.
7. The dispatch and transportation of pharmaceutical products should be undertaken only after the receipt of a valid delivery order or material replenishment plan, which should be documented.
8. There should be documented, detailed procedures for the dispatch of products.
9. Written procedures for the dispatch of pharmaceutical products should be established. Such procedures should take into account the nature of the product as well as any special precautions to be observed. Pharmaceutical products under quarantine will require release for dispatch by the person responsible for quality.
10. Records for the dispatch of pharmaceutical products should be prepared and should include at least the following information:
    - date of dispatch.
    - complete business name and 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).

11. 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.

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

16. Product recall

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

17. Annex I: Storage and labeling conditions

1. Normal Storage Conditions

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

2. Defined Storage Instructions

Pharmaceutical 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 recommended limits for descriptive storage conditions:

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	–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 well-ventilated premises at temperatures of between 15 °C and 30 °C and no more than 60% relative humidity. Extraneous odour, other indications of contamination and intense light must be excluded.
Protect from light	To be maintained in the original manufacturer's light-resistant containers.
Chilled	5 ± 3 °C
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°
Do not store below 8°C	From +8°C to +25°C

PART III: Guidelines for good distribution practices

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.

The storage, sale and distribution of pharmaceutical products are often carried out by various companies, institutions and individuals. This document sets out appropriate steps to assist in fulfilling the responsibilities involved in the different aspects of the distribution process within the supply chain and to avoid the introduction of Substandard and falsified pharmaceutical products into the marketplace via the distribution chain. The relevant sections should be considered by various participants as applicable to the particular role that they play in the distribution of pharmaceutical products.

The nature of the risks involved is likely to be similar to that for risks encountered in the manufacturing environment, e.g., mix-ups, adulteration, contamination and cross-contamination.

Substandard and falsified pharmaceutical products are a real threat to public health and safety. Consequently, it is essential to protect the pharmaceutical supply chain against the penetration of such products. Weak points in the distribution processes of pharmaceutical products provide an avenue for Substandard and falsified pharmaceutical products as well as illegally imported, stolen and substandard medicines to enter the supply chain. This is a concern in both developed and developing countries. The methods by which such products enter the supply chain have become increasingly complex and have resulted in the development of thriving secondary and grey markets throughout the world.

The involvement of unauthorized entities in the distribution and sale of pharmaceutical products is a particular concern. Only a joint approach including all parties involved in the supply chain can be successful in the fight against Substandard and falsified pharmaceutical products and, therefore, all parties active in the market should take an active part in collaborative activities.

The guidelines can also be used as a tool in the prevention of the distribution of Substandard and falsified pharmaceutical products and as a basis for inspection of manufacturers, importers and wholesalers.

To maintain the original quality of pharmaceutical products, every party active in the distribution chain must comply with the applicable legislation and regulations. Every activity in the distribution of pharmaceutical products should be carried out according to the principles of GMP, Good Storage Practice (GSP) and Good Distribution Practices (GDP) as applicable. These guidelines do not deal with all aspects of the standards for the storage of pharmaceuticals, which are covered in the EFDA Guide to Good Storage Practices for Pharmaceuticals.

2. Objective

The objective of these guidelines is to ensure the quality and identity of pharmaceutical products during all aspects of the distribution process. These aspects include, but are not limited to, procurement, purchasing, storage, distribution, transportation documentation and record-keeping practice.

3. Scope

These guidelines are intended to be applicable to all persons and companies involved in the storage and transportation of pharmaceutical products and materials. All persons and companies including manufacturer, packagers/labelers, testers, distributors, importers, and wholesalers have the responsibility for ensuring that appropriate storage and transportation conditions are maintained from the point of manufacturing up to the delivery of the drug products to the final distribution point.

These guidelines apply equally to drugs for human and to clinical trial drugs for human use and to samples that are distributed to professionals.

4. General Guidance and Principles

1. All parties involved in the distribution of pharmaceutical products have a responsibility to ensure that the quality of those pharmaceutical products and the integrity of the distribution chain are maintained throughout the distribution process from the site of the manufacturer to

the entity responsible for dispensing or providing the product to the patient or his or her agent.

2. The principles of GDP are applicable both to pharmaceutical products moving forward in the distribution chain from the manufacturer to the entity responsible for dispensing or providing pharmaceutical products to the patient, and to products which are moving backwards in the chain, for example, as a result of a return or recall.
3. The principles of GDP should also be adhered to in the case of pharmaceutical products that are donated.
4. All entities involved in the distribution process should apply due diligence with adherence to the principles of GDP, for example, in procedures relating to traceability and in recognition of security risks.
5. There should be collaboration between all parties including governments, customs agencies, law enforcement agencies, regulatory authorities, manufacturers, distributors and other entities responsible for the supply of pharmaceutical products to patients to ensure the quality and safety of pharmaceutical products and prevent the exposure of patients to Substandard and falsified pharmaceutical products.

5. Role and Responsibilities of Distributors

1. The distributor or the organization to which the distributor belongs should be an entity that is appropriately authorized in terms of applicable regulation and directives of EFDA to perform the function(s) that it intends to perform. The distributor or the organization to which it belongs should be held accountable for the activities that it performs which relate to the distribution of pharmaceutical products.

2. Only persons or entities which are authorized to do so and/or which hold the appropriate license should be entitled to import, distribute or export pharmaceutical products.

3. Distributors or their agents may only distribute a pharmaceutical product within or to a country or territory if a marketing authorization or similar authorization has been granted, which allows the use of that pharmaceutical product in that country or territory. Holders of an authorization to distribute pharmaceutical products should obtain their supplies of

pharmaceutical products only from persons or entities which are in possession of the applicable authorization to sell or supply such products to a distributor.

4. Distributors or their agents should supply pharmaceutical products only to persons or entities which are themselves authorized to acquire such products either in terms of an authorization to act as a distributor or to sell or supply products directly to a patient or to his or her agent.
5. Some duties and responsibilities may be delegated or contracted out to suitably designated persons or entities as authorized and as necessary. Duties and responsibilities may only be delegated to entities that are suitably authorized in line with the national regulation. Duties and responsibilities should be specified in a written agreement. There should be no gaps or unexplained overlaps with regard to the application of GDP. These delegated and contracted-out activities should be documented in agreements or contracts. There should be a periodic audit of such activities with regard to application of GDP.
6. If a distributor or its agent subcontracts an activity to another entity, the person or entity to whom the activity is subcontracted must be appropriately authorized to perform the subcontracted activity and should uphold the same standards as the distributor.

6. Personnel

1. All personnel involved in distribution activities should be trained and qualified in the requirements of GDP, as applicable. Training should be based on written standard operating procedures (SOPs). Personnel should receive initial and continuing training relevant to their tasks, and be assessed as applicable, in accordance with a written training program. In addition, training of the personnel should include the topic of product security, as well as aspects of product identification, the detection of SFPP and the avoidance of SFPP entering the supply chain. A record of all training, which includes details of subjects covered and participants trained, should be kept.
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.
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. EFDA regulations, directives, and standards relating to the qualifications and experience of personnel should be adhered to.

4. Personnel dealing with hazardous pharmaceutical products (such as highly active materials, radioactive materials, narcotics, and other hazardous, environmentally sensitive and/or dangerous pharmaceutical products, as well as products presenting special risks of abuse, fire or explosion) should be given specific training.
5. Personnel involved in the distribution of pharmaceutical products should wear garments suitable for the activities that they perform. Personnel dealing with hazardous pharmaceutical products, including products containing materials that are highly active, toxic, infectious or sensitizing, should be provided with protective garments as necessary.
6. 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.
7. Procedures and conditions of employment for employees, including contract and temporary staff, and other personnel having access to pharmaceutical products, must be designed and administered to assist in minimizing the possibility of such products coming into the possession of unauthorized persons or entities.
8. Codes of practice and punitive procedures should be in place to prevent and address situations where persons involved in the distribution of pharmaceutical products are suspected of, or found to be implicated in, any activities relating to the misappropriation, tampering, diversion or Substandard and falsified pharmaceutical products of any product.

7. Premises, warehousing and storage

Good storage practices (GSP) are 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 EFDA guide to good storage practices for pharmaceuticals.

8. Storage Areas

1. Precautions must be taken to prevent unauthorized persons from entering storage areas. Employees should comply with the company policies to maintain a safe, secure and efficient working environment.
2. Storage areas should be of sufficient capacity to allow the orderly storage of the various categories of pharmaceutical products, namely commercial and non-commercial products, products in quarantine, and released, rejected, returned or recalled products as well as those suspected of being SFPP.
3. Storage areas should be designed or adapted to ensure appropriate and good storage conditions. In particular, they should be clean and dry and maintained within acceptable temperature limits. Pharmaceutical products should be stored off the floor, walls and ceiling as well as suitably spaced to permit cleaning and inspection. Pallets and shelves should be kept in a good state of cleanliness and repair.
4. Storage areas should be clean, ventilated and free from accumulated waste and vermin. Organizations in charge of distribution must ensure that premises and storage areas are cleaned regularly. There should also be a written program for pest control. The pest control agents used should be safe and there should be no risk of contamination of pharmaceutical products. There should also be a fire extinguisher.
5. There should be appropriate procedures for the clean-up of any spillage to ensure complete removal of any risk of contamination.
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. Receiving and dispatch bays should protect pharmaceutical products from the weather conditions. Receiving areas should be designed and equipped to allow incoming containers of pharmaceutical products to be cleaned, if necessary, before storage.
8. Where quarantine status is ensured by storage in separate areas, these areas must be clearly marked and access restricted to authorized personnel. Any system replacing physical quarantine should provide equivalent security. For example, computerized systems can be used, provided that they are validated to demonstrate security of access.

9. Physical or other equivalent validated (e.g., electronic) segregation should be provided for the storage of rejected, expired, recalled or returned products and suspected Substandard and falsified pharmaceutical products. The products and the areas concerned should be appropriately identified.
10. Unless there is an appropriate alternative system to prevent the unintentional or unauthorized use of quarantined, rejected, returned, recalled or suspected SFPP pharmaceutical products, separate storage areas should be assigned for their temporary storage until a decision as to their future has been made.
11. Radioactive materials, narcotics and other hazardous, sensitive and/or dangerous pharmaceutical products, as well as products presenting special risks of abuse, fire or explosion (e.g., combustible or flammable liquids and solids and pressurized gasses) should be stored in a dedicated area(s) that is subject to appropriate additional safety and security measures.
12. Pharmaceutical products should be handled and stored in such a manner as to prevent contamination, mix-ups and cross-contamination. A system should be in place to ensure that the pharmaceutical products due to expire first are sold and/or distributed first (first expiry/first out (FEFO)). Exceptions may be permitted as appropriate, provided that adequate controls are in place to prevent the distribution of expired products.
13. Broken or damaged items should be withdrawn from usable stock and stored separately. Storage areas should be provided with adequate lighting to enable all operations to be carried out accurately and safely.

9. Storage Conditions and Stock Control

1. Storage conditions for pharmaceutical products should be in compliance with the recommendations of the manufacturer.
2. Facilities should be available for the storage of all pharmaceutical products under appropriate conditions (e.g., environmentally controlled when necessary). Records should be maintained of these conditions if they are critical for the maintenance of the characteristics of the pharmaceutical product stored.
3. Records of temperature-monitoring data should be available for review. There should be defined intervals for checking temperature. The equipment used for monitoring should be

checked at suitable predetermined intervals and the results of such checks should be recorded and retained. 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. Equipment used for monitoring of storage conditions should also be calibrated at defined intervals.

4. Periodic stock reconciliation should be performed by comparing the actual and recorded stocks. This should be done at defined intervals. Stock discrepancies should be investigated in accordance with a specified procedure to check that there have been no inadvertent mix-ups, incorrect issues and receipts, thefts and/or misappropriations of pharmaceutical products. Documentation relating to the investigation should be kept for a predetermined period.
5. All product-specific monitoring records should be kept for at least the shelf-life of the stored pharmaceutical product plus one year.

10. Vehicles and Equipment

1. Defective vehicles and equipment should not be used. These should either be labelled as such or removed from service.
2. Equipment and materials used for the cleaning of vehicles should not become a source of contamination or have an adverse effect on product quality.
3. Equipment chosen and used for the cleaning of vehicles should not constitute a source of contamination. Agents used for the cleaning of vehicles should be approved by management.
4. Equipment used for monitoring conditions, e.g., temperature and humidity, within vehicles and containers should be calibrated at regular intervals. Vehicles and containers should be of sufficient capacity to allow orderly storage of the various categories of pharmaceutical products during transportation.
5. 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.

6. Special attention should be paid to the design, use, cleaning and maintenance of all equipment used for the handling of pharmaceutical products that are not in a protective shipping carton or case.
7. 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.
8. 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.
9. Vehicles should be suitable for their purpose, with sufficient space and appropriately equipped to protect medical products.
10. Vehicles used for transportation of medical products should be qualified, where applicable, to demonstrate their capability to maintain the required transport conditions. There should be a maintenance programme for the cooling/heating system.
11. Vehicles, containers and equipment should be kept free from rodents, vermin, birds and other pests. There should be written programs and records for such pest control. The cleaning and fumigation agents used should not have any adverse effect on product quality.
12. 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.
13. 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.
14. Where non-dedicated vehicles and equipment are used, procedures should be in place to ensure that the quality of the pharmaceutical product will not be compromised. Appropriate cleaning should be performed, checked and recorded. Procedures should be in place to ensure that the integrity of the products is not compromised during transportation.
15. 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 of being Substandard and falsified pharmaceutical products. Such goods should be securely packaged, clearly labeled, and accompanied by appropriate supporting documentation.

16. Where special storage conditions (e.g., temperature and/or relative humidity) different from, or limiting, the expected environmental conditions are required during transportation, these should be provided, checked, monitored and recorded. All monitoring records should be kept for a minimum of the shelf-life of the product distributed plus one year, or as required by national legislation. Records of monitoring data should be made available for inspection by the regulatory authority or other oversight body.
17. Where third-party carriers are used, distributors should develop written agreements with carriers to ensure that appropriate measures are taken to safeguard pharmaceutical products, including maintaining appropriate documentation and records. Such agreements should be in line with national and regional regulatory requirements.

11. Shipment Containers and Container Labeling

1. Pharmaceutical products should be stored and distributed in shipment containers that have no adverse effect on the quality of the products and that offer adequate protection from external influences, including contamination.
2. Shipping containers should bear labels providing sufficient information on handling and storage conditions and precautions to ensure that the products are properly handled and secure at all times. The shipment container should enable identification of the container's contents and source.
3. The need for any special transport and/or storage conditions should be stated on the shipment container label. If a pharmaceutical product is intended for transfer to areas outside the control of the manufacturer's products management system, the name and address of the manufacturer and/or marketing authorization holder, special transport conditions and any special legal requirements, including safety symbols, should also be included on the container label.
4. Normally, internationally and/or nationally accepted abbreviations, names or codes should be used in the labeling of shipment containers.

5. Special care should be taken when using dry ice in shipment containers. In addition to raising possible 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.
6. Written procedures should be available for the handling of damaged and/or broken shipment containers. Particular attention should be paid to those containing potentially toxic and hazardous products.

12. Receipt

1. Medical products should be procured from appropriately authorized suppliers.
2. Deliveries should be examined for damage, seal intactness, signs of tampering, labelling, completeness of order and other related aspects (e.g. availability of a certificate of analysis, where applicable), at the time of receiving.
3. Containers and consignments that do not meet acceptance criteria at the time of receipt should be labelled, kept separate and investigated. This includes suspected falsified products.

13. Transportation and products in transit

1. 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 supplier, distributor and recipient. In cases where the recipient notices the deviation, it should be reported to the distributor.
2. 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.
3. 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.

4. Damage to containers and any other event or problem that occurs during transit must be recorded and reported to EFDA and investigated.
5. Products in transit must be accompanied by the appropriate documentation
6. Materials and pharmaceutical products should be transported in such a way that their integrity is not impaired and that storage conditions are maintained.
7. Special care should be exercised when using dry ice in cold chains. In addition to observing safety precautions, it must be ensured that the materials or product does not come into contact with dry ice, as this may adversely affect the product quality, e.g., by freezing.
8. Vehicles and containers should be loaded carefully and systematically on a last-in/first-out (LIFO) basis, to save time when unloading, to prevent physical damage and to reduce security risks. Extra care should be taken during loading and unloading of cartons, to avoid damage.
9. 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. 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.
11. Where appropriate, the use of devices to monitor conditions such as temperature during transportation is recommended. Monitoring records should be available for review.
12. Products and shipment containers should be secured to prevent or provide evidence of unauthorized access. Vehicles and operators should be provided with additional security, as appropriate, to prevent theft and other misappropriation of products during transportation.
13. Product shipments should be secured and should include the appropriate documentation to facilitate identification and verification of compliance with regulatory requirements. Policies and procedures should be followed by all persons involved in the transportation, to secure pharmaceutical products.

14. If measures to ensure the integrity of the pharmaceutical products in transit are in place, they should be managed properly. For example, if seal control programs for transit shipment are used, numbers should be issued in a tracked and sequential manner, the integrity of seals should be monitored and numbers verified during transit and upon receipt. Written procedures should be in place for use in situations where pharmaceutical products are suspected of being or are found to be Substandard and falsified pharmaceutical products.
15. The people responsible for the transportation of pharmaceutical products should be informed about all relevant conditions for storage and transportation. These requirements should be adhered to throughout transportation and at any intermediate storage stages.
16. 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 environmental conditions are maintained, e.g., using cold chain for thermos-labile products.
17. The required storage conditions for pharmaceutical products should be maintained within acceptable limits during transportation. If a deviation has been noticed during transportation by the 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. Where necessary, the manufacturer of the pharmaceutical product should be contacted for information about appropriate steps to be taken.
18. Where special conditions are required during transportation that are different from or limit the given environmental conditions (e.g., temperature and humidity), these should be provided by the manufacturer on the labels, monitored and recorded.

19. Written procedures should be in place for investigating and dealing with any failure to comply with storage requirements, e.g., temperature deviations.
20. Transportation and storage of pharmaceutical products containing hazardous substances, such as toxic or radioactive material, and other dangerous pharmaceutical products presenting special risks of abuse, fire or explosion (e.g., combustible or flammable liquids, solids and pressurized gases) should be stored in safe, dedicated and secure areas, and transported in safe, suitably designed, secured containers and vehicles. In addition, the requirements of applicable international agreements and national legislation should be met.
21. Products containing narcotics and other dependence-producing substances should be transported in safe and secure containers, and vehicles and be stored in safe and secure areas. In addition, transport should comply with applicable international agreements and national legislation.
22. Spillages should be cleaned up as soon as possible to prevent possible contamination, cross-contamination and hazards. Written procedures should be in place for the handling of such occurrences.
23. 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 Substandard and falsified pharmaceutical products. The products should be appropriately identified, securely packaged, clearly labeled and be accompanied by appropriate supporting documentation.
24. The interiors of vehicles and containers should remain clean and dry while pharmaceutical products are in transit. Packaging materials and shipment containers should be of suitable design to prevent damage of pharmaceutical products during transport. Seal control programs should be in place and managed properly.
25. Drivers of vehicles should identify themselves and present appropriate documentation to demonstrate that they are authorized to transport the load.
26. 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.
27. Pharmaceutical products in transit must be accompanied by the appropriate documentation.

PART-IV: Introduction to pharmaceutical products recall guidelines

1. Introduction

Ensuring the safety, efficacy and quality of pharmaceutical products is a prime responsibility of the manufacturers and distributors (e.g., Importers) of medicines. The responsibility is shared with the Ethiopian Food Medicine and Healthcare Administration and Control Authority (EFDA). When pharmaceutical products are suspected of being potentially harmful to users due to their defective quality, safety or efficacy, they may be subjected to a recall and all related information must be report to Ethiopian Food and Drug Authority (EFDA).

These Guidelines are recognized as being appropriate to the specialized requirements for the recall of pharmaceutical products and are the licensing conditions for all licenses issued by EFDA. For any Licensee that has failed to comply with those conditions, EFDA may revoke or suspend the license for a period of time that it believes appropriate.

The role of EFDA in a recall is to assess the adequacy of the Licensee's decision on the recall of the product and, should action be taken, to monitor the progress and effectiveness of the recall. EFDA may alert the public of the problem with the specified product and instruct the Licensee to recall and dispose of the product according to the circumstances. The recall might be initiated by the manufacturer, wholesaler or license holder, or by EFDA.

2. Objective

The Pharmaceutical Products Recall Guidelines (the "Guidelines") are intended to ensure that, in the event of a necessary recall, recall operations are effectively and efficiently carried out by the manufacturer, importer, distributor or market authorization holder of the pharmaceutical product (hereafter known as the "Licensee") in order to safeguard public health.

3. Steps of recall procedure

The procedure is divided into six steps, which are set out below:

4. Receipt of Pharmaceutical Product Problem Report

Notification to EFDA (see also Pharmaceutical Product Problem Report Form, Part 1 (Appendix I)

1. Initiation of a Recall/Information Required for Assessment of Recall

Information on product, problem and distribution is required; see also Recall Notification Form, Part 2 (Appendix I)

2. Assessment of Recall

   The classification, level and strategy of recall are determined depending on the potential hazard of the defective product and the extent of product distribution.

3. Communication

   Letters and press release (if required) are dispatched to relevant firms for notifying on the recall. See the Recall Reply Format (Appendix II).

4. Progress of Recall and Report

   Progress reports and a final report are submitted EFDA. See the Final Report Form (Appendix III).

5. Evaluation of the Recall

   The effectiveness of the recall is monitored by EFDA.

5. Notification of a pharmaceutical problem

A recall might be initiated as a result of reports or complaints on quality, safety or efficacy of a pharmaceutical product referred to the Licensee from a variety of sources — manufacturers, wholesalers, medicine retail outlets, health institutions, health professionals, research institutes, or patients. A recall might also be initiated as a result of analysis and testing of samples of pharmaceutical products by the manufacturer and/or EFDA. A recall of pharmaceutical products manufactured overseas might be initiated by the local or overseas health authorities, or from information received directly from such authorities and international organization such As World Health Organizations (WHO).

Certain information is essential to permit the assessment of the validity of the report of quality defects, safety or efficacy problem with pharmaceutical products, the potential danger to consumers and the action appropriate to the situation. A Pharmaceutical Product Problem Report Form (Part 1) is used to report problems to EFDA (see Appendix I).

Serious problems, such as those that may lead to the recall of Class I or Class II products must be reported to EFDA within 24 hours after receipt of the complaint or report for investigation. The Pharmaceutical Product Problem Report Form (Part 1), together with opinions on toxicological or therapeutic hazards and the action proposed by the authority or organization (if any), should be referred to the concerned directorate of EFDA for handling such issues. For less serious problems, such as those that would result in a Class III recall, the Pharmaceutical Product Problem Report

Form (Part 1) should be sent to EFDA no later than 72 hours after receipt of the complaint or report of a problem. (Refer to "Classification of Recalls" in the "Assessment of Recall" section below.)
It should be noted that the Licensee must send the Pharmaceutical Product Problem Report Form (Part 1) to EFDA *prior* to making a decision to recall.
When the need for recall has been established, additional information is required so that an appropriate recall strategy may be devised. A summary of the information required is provided in the following section.

6. Initiation of recall and information required for assessment

When the Licensee decides to initiate a recall on a pharmaceutical product, it must notify EFDA of the recall situation using the Recall Notification Form, Part 2 of the Pharmaceutical Product Problem Report Form (Appendix I). Immediately after making the decision to recall and notifying the concerned directorate of EFDA, the Licensee and other organization involved in distribution must submit the information outlined below. Contact information for the concerned directorate of EFDA is provided by EFDA on the reporting form. The Licensee should submit the available information to EFDA as soon as the recall decision is made, rather than waiting until all applicable information is prepared and assembled. This "early" notification is necessary to allow EFDA to review and comment on the written notification and to offer guidance and assistance in the recall process.

The information required may include:

Details of the Problem

- Name and contact information (telephone and fax numbers) of the person reporting the problem;
- Date of report;
- Physical location of the problem;
- Nature of the problem;
- Number of similar reports received (if any); and
- Results of tests and other investigations on the suspect or other samples.

Details of the Product

- Name of the product and description, including active ingredients, dosage form, strength, registration number, and package size or type;
- Batch number(s) and expiry date;
- Manufacturer/distributor name(s), contact information (telephone and facsimile numbers) and email address;

- Date manufactured and date released or imported to Ethiopia;
- Quantity of the batch, date and amount manufactured,
- Local distribution list;
- Overseas distribution list, if product exported from Ethiopia; and
- Whether the product is meant to be sterile.

Health Hazard Evaluation and Proposed Action

- Type of hazard and evaluation of health hazard to user;
- Action proposed by the Licensee;
- Proposed recall classification and level; and
- Availability of an alternative product.

7. Role and responsibilities of stakeholders

1.EFDA can initiate a recall or approve a recall initiated by a manufacturer, importer or distributor. Although EFDA initiates or approves the recall, the product owner (manufacturer, importer, etc.) is responsible for implementing the recall process.

2.Regional/city administration regulatory bodies

— Should cooperate in the implementation of a recall initiated by EFDA or a pharmaceutical manufacturer or importer, etc.

— Should also report pharmaceutical quality problems to EFDA.

3.Pharmaceutical manufacturers, importers and organization involved in the distribution

— Should have their own recall Standard Operating Procedures (SOPs)

— Should notify EFDA of recall initiation.

— Should conduct an effective recall in consultation with EFDA.

— Should assess the effectiveness of the recall and report any recall they made to EFDA.

4.Wholesalers

— Should cooperate in any recall conducted by EFDA, manufacturers, importers and distributors.

— Should develop their own recall SOPs.

5.Health facilities (hospitals, clinics, health centers, etc.)

— Should cooperate in the implementation of any recall initiated by EFDA, manufacturers, importers and distributors.

6.Medicine retail outlets

— Should cooperate in the implementation of any recall initiated by EFDA, manufacturers, importers and distributors.

7.Healthcare professionals

— Should cooperate in the implementation recall initiated by EFDA, manufacturers, importers and distributors.

8. Recall strategy

Each recall is a unique exercise; however, there are a number of factors common to all recalls that must be considered in tailoring an appropriate recall strategy. These include the nature of the deficiency in the product, the incidence of complaints, public safety, distribution networks, recovery procedures, resources for corrective action and availability of alternative products.

In determining the recall strategy, the Licensee should consider the factors which may affect the duration of the recall action and should inform EFDA. The recall should be completed by the date directed by EFDA.

When the required information is available (see section above on "Initiation of Recall and Information Required for Assessment"), the Licensee should propose an appropriate recall strategy to EFDA; and EFDA must approve to the proposed recall strategy before it can be implemented. Implementation of the recall should follow the basic steps summarized in Section II and these will be common to all strategies.

In its recall strategy, the Licensee should address the following points:

- Indicate the proposed level in the distribution chain to which the recall will extend (see Level of Recall below). If the recall extends solely to the wholesale level, the rationale for not recalling to the retail level should be explained.
- In case of a recall to the consumer level, additional information should be included:
  - Location of recall spots for consumers (preferably, no fewer than 10 recall spots covering various regions of Ethiopia), their operating hours and duration (minimum of seven (7) days);
  - Hotlines number(s) for inquiries and corresponding operating hours; and
  - Proposed refund mechanism at the recall spots, conditions of refund (e.g., applicable to opened products, expired products or parallel-imported products) and methods of refund (e.g., cash, credit notes or product replacement, etc.);
- Indicate the method of notification (e.g. mail, phone, facsimile, email).
- Indicate how the recall message will be delivered to customers, e.g., press release or recall letter, etc.

- If the Licensee has a website, it should consider posting the recall notification on the website as an additional method of recall notification.
- Indicate what customers have been instructed to do with the recalled product.
- Provide the name, title and contact information of the recall contact person for each of the recalling firm's consignees. Addressing a recall letter to a recall contact person will expedite the recall process and reduce the potential for the recall letter being misdirected.
- If product is to be returned, explain the mechanics of the process.
- Explain if the recall will create a market shortage that may impact the consumer.

9. Classification of Recall

Recalls are classified according to the following system:

Class I Recall

Class I indicates the product to be recalled is potentially life-threatening or could cause a serious risk to health.

Examples of Class I defects include:

- Wrong product (label and contents are from different products)
- Correct product but wrong strength, with serious medical consequences
- Microbial contamination of sterile injection or ophthalmic product
- Chemical contamination with potentially serious medical consequences
- Mix-up of products ("rogues") with more than one container involved
- Wrong active ingredient in a multi-component product with serious medical consequences.

Class II Recall

Class II indicates the product to be recalled contains defects that could result in illness or improper treatment, but the consequences would not be as serious as in Class I. It is a situation in which the use of or exposure of the product in question may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote.

Examples of Class II defects include:

- Mislabeling, e.g., wrong or missing text or figures
- Missing or incorrect information in leaflets or inserts
- Microbial contamination of non-injectable, non-ophthalmic product with potential medical consequences
- Chemical/physical contamination (significant impurities, cross-contamination, particulates)

- Mix-up of products in containers ("rogues")
- Non-compliance with specifications (e.g., assay, stability, fill/weight or dissolution)
- Insecure closure with potentially serious medical consequences (e.g., cytotoxics, child-resistant containers, potent products).

Class III Recalls

Class III indicates the product to be recalled contains defects that may not pose a significant hazard to health, but withdrawal may be initiated for other reasons.

Examples of Class III defects include:

- Faulty packaging, e.g., wrong or missing batch number or expiry date
- Faulty closure
- Contamination – microbial, spoilage, dirt or detritus, particulate matter.

Class I or Class II recalls are considered to be urgent, safety-related recalls. They must be reported to FMAHCA for further evaluation and investigation.

Class III recalls are considered to be non-safety-related recalls.

Note: Each recall is a unique exercise; there may be occasions when the scope of a recall can be narrowed to particular customer groups. EFDA determines the classification and may seek expert advice when the nature of the hazard or its significance is not clear.

10. Level of Recall

As it does with the classification of a recall, EFDA assigns the level (or depth) of a recall. The principal factors to be considered in determining the recall level are the significance of the hazard (if any), the channels by which the pharmaceutical products have been distributed, and the level to which distribution has taken place. Again, EFMAHCA may seek expert opinions to determine the significance of the hazard.

There are three levels of recall: Wholesale, retail and consumer.

Wholesale Level: This level includes:

- All parties involved in wholesale distribution, which may include the importer, wholesalers and retail pharmacies.

Retail and health Institution Level: This level includes:

- All public and private hospital pharmacies;
- Health facilities
- Retail pharmacies;
- Clinical investigators and the institutions in which clinical investigations are performed;
- Medical, dental and other health care practitioners;
- Nursing homes and other related institutions;
- Other retail outlets, e.g., medicine shops, supermarkets and health food stores; and
- Wholesale level.

Consumer Level: This level includes:

- Patients and other consumers; and
- Wholesale and retail levels.

11. Communication to firms and public

Recall Letter

In case of a recall, the Licensee and other organization involved in the distribution may prepare letters with a factual statement of the reasons for the recall of the product, together with specific details that will allow the product to be easily identified. The letter may be sent by mail, facsimile or e-mail to clients.

The recall letter should appear on organization letter head and include the date as well as the name and title of the signatory. The text of recall letter may include:

1. Description of the pharmaceutical product: Name of the product; marketing authorization number in Ethiopia; name of the manufacturer, package size; strength; dosage form; batch number(s) and expiry date;
2. Hazards associated with the product: The reason for the recall should be explained concisely, and state clearly that further distribution or use of the product should cease immediately.
3. Instructions for recall of the product: The method of return, disposal or correction and refund mechanism of the product should be detailed. There should be a request for a response to confirm receipt and understanding of the action to be taken, e.g., pre-addressed cards, telephone replies or a form to complete and return by fax number or e-mail.

For a Retail and health institution Level recall, the Licensee should have a method of confirming the return of all stock on hand from consignees and report returns using the Recall Reply Format (Appendix II).

If safety to the public is involved and the distribution is limited, the Licensee may contact the clients of the information listed above by telephone and followed by a recall letter.

Public Warning

The purpose of public warning is to alert the public rapidly that a pharmaceutical product being recalled presents a serious health hazard. It is reserved for urgent situations, where other means for preventing the use of recalled product appear inadequate. EFDA in consultation with the recalling firm will ordinarily issue such publicity.

The recalling firm that decides to issue its own public warning is requested to submit its proposed public warning and plan for distribution of the warning for review and comment by EFDA.

The recall strategy will specify whether a public warning is needed, and it will issue as:

1. General public warning through the general news media, either national or local as appropriate;
2. Public warning through specialized news media e.g. professional or trade press (if any), or to specific segment of the population such as pharmacists, physicians, hospitals etc.

Rapid alert to the public is usually reserved for hazards classified as Class I and, where appropriate, Class II, or situations where other means for controlling the hazard appear inadequate.

12. Responsibilities of licensees

The Licensee has responsibilities related to recall of pharmaceutical products in areas:

1. Maintaining records and establishing procedures that will assist in facilitating a recall.
2. Taking the prime responsibility for implementing recall in the situation where it is necessary.
3. The licensee should maintain records for all the pharmaceutical products manufactured or distributed by them in accordance with the following guidelines:

For Manufacturers:

— A system should be in operation whereby the complete and up-to-date histories of all batches of products from the starting materials to the finished products are progressively recorded.

— The system should allow for determination of the utilization and disposal of all starting materials and bulk products.

For Distributors:

— Records of all sales or distribution (including professional samples and export to overseas countries) of pharmaceutical products should be retained or kept readily accessible to permit a complete and rapid recall of any lot or batch of a pharmaceutical product.

In addition, the Licensee should retain records of problem reports received about each product. Problem reports should be evaluated by competent personnel and appropriate action taken. The evaluation of each report and the action taken should be shown in the records.

All the above records should be readily available and easy to follow so as to expedite a recall whenever necessary. A copy of manufacturing/import and distribution records should be sent to EFDA when a recall is implemented.

Problem Reporting

Where evaluation of a problem report concerning pharmaceutical products, including pharmaceutical products that have been exported, indicates that a recall may be necessary, the report must be conveyed with the least possible delay to EFDA. Any batch of a formulated product that has been distributed, or any batch of starting material that is found not to comply with the approved product specifications or relevant standards must also be reported if it has been used in distributed products.

The Licensee has the prime responsibility for implementing recall action, and for ensuring compliance with the recall procedure at its various stages; however, no recall, regardless of level, should be undertaken without consultation with EFDA.

A responsible officer for recall should be appointed to coordinate the recall and his/her name and contact telephone number should be provided to EFDA. In addition, this officer must regularly report the progress of the recall to EFDA.

For a Class I recall, the Licensee should notify its clients within 24 hours upon the decision to recall. The company personnel may be utilized to immediately disseminate information on the recall. This includes telephone advice to quarantine stock pending recall or possible recall, followed by recall letters if necessary. A Recall Reply Form (Appendix II) should be sent to all consignees to confirm the quantity of stock they have on hand and to have all of that stock returned. The Recall Reply Form should be kept for inspection by EFDA. All Class I recalls should be completed within the time frame found suitable for the case as agreed by EFDA.

For a Consumer Level recall, the Licensee should set up sufficient recall spots for collection of recalled products. Information about the locations of the recall spots, operating hours and duration, and conditions and method of refund should be presented to consumers by effective means.

Company representatives may be utilized to recover stock that is the subject of recall, providing the provisions are observed in relation to unauthorized possession of certain stock, e.g., dangerous drugs.

The Licensee may also be required to notify overseas recipients of recall actions that affect them.

Refund Mechanism

The Licensee should set up a refund mechanism for the recalled products.

Post-recall

The Licensee is expected to provide EFDA with a report on the progress of the recall within seven (7) days of initiation of the recall. This interim report should contain the following information:

- Number of organizations or persons to whom the defective product has been supplied;
- Date and means of notifying them of the recall;
- Number of responses received from them;
- Names of the non-responders;
- Quantity of stock returned;
- Quantity of stock that has been taken off shelves pending return to Licensee; and
- Estimated timeframe for the completion of the recall.

Using the Final Report Form (Appendix III), a final report should be submitted to EFDA within 14 days after commencement of the recall that contains the following information:

- Circumstances leading to the recall;
- Consequent action taken by the Licensee;
- Extent of distribution of the relevant batch in Ethiopia and overseas;
- Result of the recall —
  - quantity of stock returned, corrected, outstanding,
  - quantity of stock used by the consignees,
  - quantity of stock not located, and
  - date of recall completion;
- Confirmation, where practicable, that retailers have returned all recalled products to the Licensee and the customers have received the recall letter, using Recall Reply Form (Appendix II); and

If the final report cannot be submitted within 14 days after commencement of the recall, the Licensee should report to EFDA with a relevant explanation and obtain its approval for the delay.

After completion of the recall, a report on the results of the investigation of the problem and the action(s) proposed to be implemented to prevent a recurrence of the problem should be submitted to EFDA in a timely manner.

These reports establish the effectiveness of the recall and, unless satisfactory reports are received, further recall action may have to be considered.

13. Evaluation of recall

The evaluation consists of a check on the effectiveness of the recall and an investigation of the reason for the recall as well as the remedial action taken to prevent a recurrence of the problem.
Check on the Effectiveness of Recall Action

The Licensee will assume full responsibility for assuring that the recall is effective.
EFDA examines the recall reports, and the signed Recall Reply Forms submitted by the Licensee and assesses the effectiveness of the recall action. Recall records may be inspected and, in some cases, EFDA may contact a percentage of customers in the distribution list as a means of assuring that the Licensee is carrying out its recall responsibilities. If EFDA finds the recall to be ineffective, the Licensee will be asked to take appropriate steps, including re-issuing recall letters.

Investigation of Reasons for Recall and Initiation of CAPA

Upon completion of a recall, the Licensee is asked to provide a report on the investigation of the problem and details of corrective and preventive actions (CAPA) proposed to prevent a recurrence of the problem that gave rise to the recall. Where the nature of the problem and appropriate CAPA are not apparent, investigation and, in some cases, an inspection of good manufacturing practices may be necessary.

Resuming Supply

The quality of the product must conform to specific requirements before resuming its supply to public. The Licensee must seek approval from EFDA for reinstatement of the pharmaceutical product previously recalled.

Implementation of CAPA

The Licensee shall identify the root cause of the problem and implement the corrective and preventive action accordingly to prevent the occurrence of problems in the future.

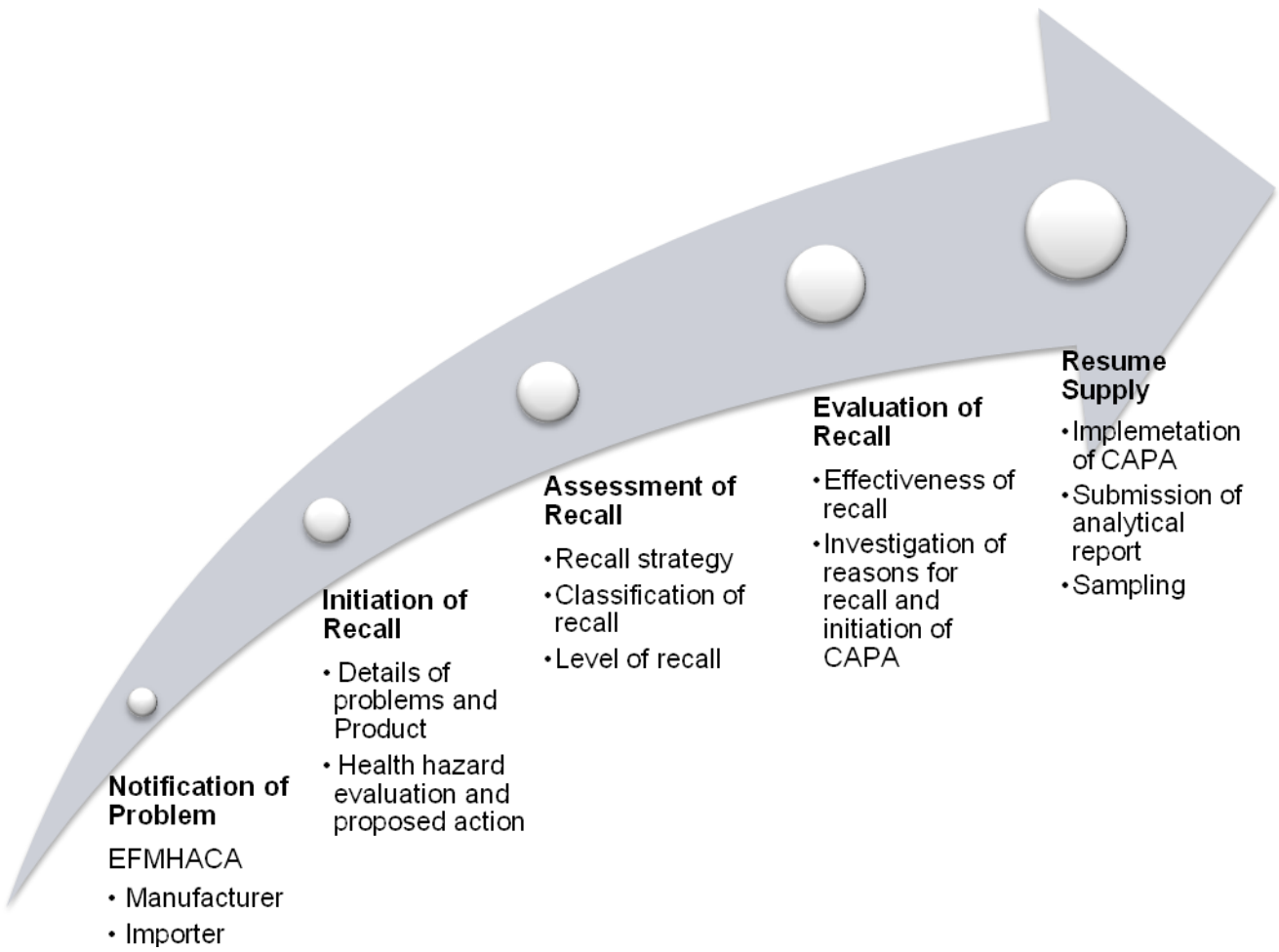
Submission of Analytical Report

After implementing the CAPA and subsequently manufacturing or importing a new batch of the product, the Licensee shall submit an analytical report(s) to EFDA of the new batch as tested by an external ISO accredited or WHO prequalified laboratory as a proof of product quality. EFDA will evaluate the submitted report(s) and, in turn, will inform the Licensee whether the submitted reports are satisfactory. The documents relating to submission of an analytical report are summarized in Appendix IV.

Sampling

When EFDA is satisfied with the submitted reports, it will collect samples of the first batches of the product (being manufactured by the local manufacturer or being imported) for examination. If the Licensee is a local manufacturer, it shall notify EFDA once the product is ready for sampling. If the product is imported, samples will be collected from the consignment and the consignment will be marketed after the EFDA laboratory test results are found to be satisfactory. The product can be put on the market only after approval for reinstatement has been obtained from EFDA.

14. Flow chart of the recall process



15. Appendix I: Pharmaceutical Product Reporting Form (Part I) and Recall Notification Form (Part II)

Note:

Part 1 of this form should be used to report a problem with pharmaceutical products in quality, safety or efficacy, which are thought to have arisen during their manufacture, storage, or handling. Problems of this nature may require laboratory investigation by EFDA.

Part 2 of this form should be completed when a decision of recall is established.

When the reported problem may lead to a Class I or II recall, it should be reported to the designated EFDA pharmacist by telephone within 24 hours and followed by facsimile or email of Part 1 of this form.

If a Class I or II recall is required, Parts 1 and 2 of this form should be reported to the designated EFDA pharmacist immediately by telephone and followed by facsimile or email.

The Licensee should submit the available information to EFDA as soon as the recall decision is made, rather than waiting until ALL applicable information in Part 2 of this form is prepared and assembled.

For a problem that may lead to a Class III recall, Part 1 of this form should be reported to the designated EFDA pharmacist by facsimile or email within 72 hours.

If a Class III recall is required, Parts 1 and 2 of this form should be submitted by facsimile or email to the designated EFDA pharmacist.

Contact information for the designated EFDA pharmacist:

Tel: _____

Email: _____

Fax Number: _____

Use a separate form for each pharmaceutical product reported.

Pharmaceutical Product Problem Report Form (Part I)

<table>
<tr><td colspan="5">DETAILS OF THE PROBLEM</td></tr>
<tr><td colspan="5">Reporting company:</td></tr>
<tr><td colspan="2">Name of contact:</td><td colspan="3">Position /Occupation:</td></tr>
<tr><td colspan="5">Name of the organization;</td></tr>
<tr><td colspan="5">Address;</td></tr>
<tr><td colspan="5">Email:</td></tr>
<tr><td colspan="2">Tel (office):</td><td colspan="3">Fax:</td></tr>
<tr><td colspan="5">Mobile</td></tr>
<tr><td colspan="5">Pharmaceutical product problem occurred in Ethiopia? If not, location of the problem:</td></tr>
<tr><td colspan="5">Nature of the problem:</td></tr>
<tr><td colspan="5">Date of compliant received:</td></tr>
<tr><td>Source of compliant</td><td>Patient □</td><td>Customer □</td><td>Retailer □</td><td>Self-inspection □</td></tr>
<tr><td></td><td colspan="4">Other (specify)</td></tr>
<tr><td colspan="5">Number of similar reports received:</td></tr>
<tr><td colspan="5">Description of the problem (use separate sheet if this space is not enough</td></tr>
<tr><td colspan="5">Results of tests/investigation on the suspect product or other samples</td></tr>
</table>

Has the manufacturer or distributor been contacted? Yes □ No □ (If yes, please provide company names)
Other relevant information (Attach photo, package insert, and press release of any overseas authority of the product if any)

<table>
<tr><td colspan="5">DETAILS OF THE PRODUCT</td></tr>
<tr><td colspan="2">Name of the product (on marketing authorization certificate):</td><td colspan="3">Ethiopian Registration Number:</td></tr>
<tr><td colspan="5">Active ingredient and strength:</td></tr>
<tr><td colspan="5">Indications (Attach additional sheet if this space is not enough):</td></tr>
<tr><td colspan="2">Dosage form:</td><td colspan="3">Pack size:</td></tr>
<tr><td colspan="2">Batch number:</td><td colspan="3">Expiry date:</td></tr>
<tr><td rowspan="3">Distribution of Products:</td><td>Wholesalers ☐</td><td>Hospitals ☐</td><td colspan="2">Health centers ☐</td></tr>
<tr><td>Pharmacies ☐</td><td>Drug stores ☐</td><td colspan="2">Rural drug vendors ☐</td></tr>
<tr><td>Clinics ☐</td><td colspan="3">Others ☐ (Specify)</td></tr>
<tr><td colspan="5">Manufacturer</td></tr>
<tr><td colspan="5">Name:</td></tr>
<tr><td colspan="5">Address:</td></tr>
<tr><td>Tel (office):</td><td colspan="2">Fax:</td><td colspan="2">Manufacture date:</td></tr>
<tr><td>Batch Size:</td><td colspan="4">Quantities of batches manufactured:</td></tr>
<tr><td colspan="2">Date and quantity released:</td><td colspan="3">Quantity on hold:</td></tr>
<tr><td rowspan="2">Quantity distributed</td><td colspan="4">Local:</td></tr>
<tr><td colspan="4">Overseas:</td></tr>
<tr><td colspan="5">Importer</td></tr>
<tr><td colspan="5">Name:</td></tr>
<tr><td colspan="5">Address:</td></tr>
<tr><td>Tel (office):</td><td colspan="2">Fax:</td><td colspan="2">Import date:</td></tr>
<tr><td colspan="2">Quantity of the batch imported:</td><td colspan="3">Quantity on hold:</td></tr>
<tr><td colspan="5">Date and quantity released:</td></tr>
<tr><td rowspan="2">Quantity distributed:</td><td colspan="4">Local:</td></tr>
<tr><td colspan="4">Re-exported:</td></tr>
<tr><td colspan="5">Local Distributor (Please attach distribution list.)</td></tr>
<tr><td colspan="5">No. of local distributors:</td></tr>
<tr><td colspan="5">Name</td></tr>
<tr><td colspan="5">Address</td></tr>
<tr><td colspan="2">Contact person</td><td colspan="3">Tel (office):
Tel (mobile):</td></tr>
<tr><td colspan="2">Quantity on hold:</td><td colspan="3">Quantity distributed:</td></tr>
<tr><td colspan="5">Exporter</td></tr>
<tr><td colspan="5">Has the product been exported? YES ☐ NO ☐</td></tr>
</table>

If yes, specify the country/countries:

Name of Reporter_____ Position _____

Contact Number _____ Date _____

Signature of the reporter _____

Recall Notification Form (Part II)

<table>
<tr><td colspan="3">RISK ASSESSMENT</td></tr>
<tr><td colspan="3">Types of Hazards: Quality ☐ Safety ☐ Efficacy ☐
Other ☐ (specify)</td></tr>
<tr><td colspan="3">Evaluation of hazards to users (i.e., effect on users, possibility of occurrence) (Attach expert advice.)</td></tr>
<tr><td colspan="3">Proposed recall classification: Class I ☐ Class II ☐ Class III ☐</td></tr>
<tr><td colspan="3">Proposed action (with agreement of EFDA):</td></tr>
<tr><td colspan="2">Recall start date:</td><td>Proposed recall end date:</td></tr>
<tr><td colspan="3">Hotline(s) for inquiries:</td></tr>
<tr><td>Hotline(S) Hours of Operation:</td><td>Mon-Fri:</td><td>Sat, Sun, public holiday:</td></tr>
<tr><td colspan="2">Responsible officer of recall:</td><td>Tel (office):
Tel (mobile):</td></tr>
<tr><td colspan="3">Proposed recall level: Wholesale ☐ Retail ☐ Customer ☐</td></tr>
<tr><td colspan="3">Locations of recall spots (for Customer Level recall only):</td></tr>
<tr><td colspan="3">Hours of operation and duration of recall spots (for Customer Level recall only)</td></tr>
<tr><td colspan="3">Means of refund at recall spots: Cash ☐ Credit Note ☐ Replacement ☐ Other □</td></tr>
<tr><td colspan="3">Conditions of refund at recall spots:</td></tr>
<tr><td colspan="3">Proposed recall strategy (Use separate sheet if this space is not enough):</td></tr>
</table>

Name of reporter _____ Position _____

Contact Number ..... Date _____

Signature of the reporter _____

16. Appendix II: Recall Reply Form

To	
Attention	
Fax/Email	
Postal Address	
Subject	
From	
Contact Person	
Telephone (office)	
Fax/Email	

We **DO☐DO NOT☐**have stock that is subject to this recall.

We have reported and returned all the stock on hand to _____.

(Licensee Name)

Stock Received:

Batch No	**Quantity**

Unused stock subject to recall (currently in quarantine):

Batch No	**Quantity**

Any other relevant details:

_____

_____

I declare that the information provided by me in this reply form is complete and true to the best of my knowledge.

Signature _____ Date _____

17. Appendix III: Final Report

Details of Recalled Product	
Product name:	Marketing Authorization Certificate No.:
Active ingredient and strength:	
Dosage form:	Package size:
Batch no.:	Expiry date:
Reason for recall:	
Extent of distribution:	
Imported/manufactured quantity:	
Quantity distributed in Ethiopia:	No. of consignees:
Quantity exported:	Countries:
Action taken by the Licensee:	
Result of recall:	
Returned quantity:	Outstanding quantity:
Used or sold quantity by the consignees:	
Quantity of stock not located:	
No. of Recall Reply Forms received from consignees on all stock returned/reported:	
Disposal Plan: Destroy ☐ Return to overseas manufacturer ☐ Other ☐(please specify):	
Details of disposal method:	

Name of reporter _____ Position _____

Contact Number: _____. Date _____

Signature of the reporter _____

18. Appendix IV: Document related to submission of analytical report

Accredited Test

The laboratory performing the tests should obtain accreditation on the specific test method in accordance with the international standards, e.g., ISO 17025. The Licensee shall submit the raw data and quality control data for the tested samples to substantiate the validity of test results. These data could facilitate the evaluation of the test result by the EFDA laboratory.

Non-Accredited Test

In case accreditation of the specific test could not be arranged, the analytical report might be considered acceptable if the laboratory has obtained appropriate accreditation in the area of pharmaceuticals or pharmaceutical products and be able to provide necessary documentation to prove its competence in respect to its quality control and technical aspects in performance of the specific chemical tests.

Basically, the information should include, but is not limited to, the following:

- Detailed method (including standard preparation procedure, sample preparation procedure, instrument parameters, and quality control procedure);
- Raw data and quality control data for all tested samples shown in the report (including chromatograms, mass spectra and calculation);
- Validation summary for the method used (including method linearity, limit of detection, limit of quantitation, method bias, precision, and measurement uncertainty);
- Reference material used and purity verification summary; and
- Relevant proficiency test participation.

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