FOOD, MEDICINE AND HEALTH CARE ADMINISTRATION AND CONTROL AUTHORITY OF ETHIOPIA (EFMHACA)

GUIDELINES FOR:

GOOD STORAGE PRACTICES

GOOD DISTRIBUTION PRACTICE

PHARMACEUTICAL PRODUCT RECALL

First Edition

September, 2015

Addis Ababa, Ethiopia

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FOOD, MEDICINE AND HEALTH CARE ADMINISTRATION AND CONTROL AUTHORITY OF ETHIOPIA (EFMHACA)

PART I
GUIDELINES FOR GOOD STORAGE PRACTICES

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ACRONYMS

API	Active Pharmaceutical Ingredient
EFMHACA	Ethiopian Food, Medicine and Healthcare Administration and Control 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 Medicines Program
SOP	Standard Operating Procedure
USAID	United States Agency for International Development
USP	U. S. Pharmacopeial Convention
WHO	World Health Organization

ACKNOWLEDGEMENT

The Food, Medicine and Healthcare Administration and Control Authority (EFMHACA) of Ethiopia would like to acknowledge and express its appreciation to the United States Agency for International Development (USAID) and U.S. Pharmacopeial Convention (USP) Promoting the Quality of Medicines (PQM) Program for the financial and technical support delivered in preparation of these *Guidelines for Good Storage Practices*. EFMHACA would like also to acknowledge all institutional participants of the workshop held to enrich these guidelines.

1. INTRODUCTION

EFMHACA 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 Food, Medicine and Healthcare Administration and Control Authority of Ethiopia (EFMHACA) 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. DEFINITIONS

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

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

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

Excipient: A substance other than the active ingredient that 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.

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.

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.

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

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

Pharmaceutical product: Any 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.

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

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

Supplier: A person or entity providing pharmaceutical products and materials upon request. Suppliers may be agents, brokers, distributors, manufacturers or traders. Where applicable, suppliers should be authorized by a competent authority.

5. PERSONNEL

5.1 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. EFMHACA regulations on qualifications requirements should be followed.

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

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

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

5.5 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.

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

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

5.8 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.

6. PREMISES AND FACILITIES

Premise and other areas utilized for storage purposes should comply with the minimum standards set by EFMHACA. They 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.

Storage Areas

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

6.2 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.

6.3 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.

6.4 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.

6.5 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.

6.6 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.

6.7 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.

6.8 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.

6.9 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.

6.10 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.

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

6.12 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.

6.13 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.

6.14 Narcotic drugs and other controlled materials and pharmaceutical products should be stored in compliance with international conventions, and national laws and regulations on narcotics.

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

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

Storage Conditions

6.17 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.

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

Monitoring of Storage Conditions

6.19 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.

6.20 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.

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

7. STORAGE REQUIREMENTS

Documentation: Written Instructions and Records

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

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

7.3 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.

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

8. CONTAINER AND LABELING

8.1 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.

8.2 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.

9. RECEIPT OF INCOMING MATERIALS AND PHARMACEUTICAL PRODUCTS

9.1 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.

9.2 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.

9.3 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.

9.4 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.

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

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

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

10. STOCK ROTATION AND CONTROL

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

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

10.3 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.

10.4 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.

11. CONTROL OF OBSOLETE AND OUTDATED MATERIALS AND PHARMACEUTICAL PRODUCTS

11.1 All stocks should be checked regularly for obsolete and outdated materials and pharmaceutical products.

11.2 All due precautions should be observed to prevent the issue of outdated materials and pharmaceutical products.

12. MANAGEMENT OF RETURNED GOODS

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

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

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

13. DISPATCH AND TRANSPORT

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

13.2 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.

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

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

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

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

13.7 Records for dispatch should be retained, stating at least the:

- Date of dispatch;
- Customer's name and address;
- Product description, e.g., name, dosage form and strength (if appropriate), batch number, expiry date and quantity; and
- Transport and storage conditions.

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

14. 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.

15. REFERENCES

1. Good trade and distribution practice (GTDP) of pharmaceutical starting materials. Geneva, World Health Organization, 2002 (unpublished document QAS/01.014; available upon request from the Office of Essential Drugs and Medicines Policy, World Health Organization, 1211 Geneva 27, Switzerland).
2. Guidelines for Good Storage Practices in medical stores and hospitals, Central Administration of Pharmaceutical Affairs, Ministry of Health and Populations, 2004.
3. Good distribution practices (GDP), National Pharmaceutical Control Bureau, Ministry of Health, Malaysia, 2nd edition, 2013. In: Good manufacturing practices for pharmaceutical products. In: Quality assurance of pharmaceuticals. A compendium of guidelines and related materials. Volume 2. Good manufacturing practices and inspection. Geneva, World Health Organization, 1999.

ANNEX I: STORAGE AND LABELING CONDITIONS

1. Normal Storage Conditions

Storage should be dry, well-ventilated premises at temperatures of 15–25°C or, 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 labeling instructions is recommended:

On the label	**Means**
Do not store over 30°C	From +2°C to +30°C
Do not store over 25°C	From +2°C to +25°C
Do not store over 15°C	From +2°C to +15°
Do not store over 8°C	From +2°C to +8°C
Do not store below 8°C	From +8°C to +25°C
Protect from moisture	No more than 60% relative humidity in normal storage conditions; to be provided to the patient in a moisture-resistant container
"Protect from light"	To be provided to the patient in a light-resistant container
Freeze/Freezer	The temperature is thermostatically controlled between -20°C and -10°C
Refrigerator	The temperature is thermostatically controlled between 2°C and 8°C
Cold place	The temperature does not exceed 8°C
Cool place	The temperature is between 8°C and 15°C
Room temperature	The temperature is between 15°C and 30°C

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PART II
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GSP	Good Storage Practices
GTDP	Good Trade and Distribution Practices
PQM	Promoting the Quality Medicines Program
SFFC	Spurious/ Falsely-labelled/falsified/Counterfeit
SOP	Standard Operating Procedure
USAID	United States Agency for International Development
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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 Spurious/falsely-labelled/falsified/counterfeit medicines 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.

Spurious/falsely-labelled/falsified/counterfeit 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 Spurious/falsely-labelled/falsified/counterfeit 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 Spurious/falsely-labelled/falsified/counterfeit 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 Spurious/falsely-labelled/falsified/counterfeit 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 EFMHACA *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. DEFINITIONS

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

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: A business agreement for the supply of goods or performance of work at a specified price.

Spurious/falsely-labelled/falsified/counterfeit pharmaceutical product: A pharmaceutical product that is deliberately and fraudulently mislabeled with respect to identity and/or source. Spurious/falsely-labelled/falsified/counterfeiting can apply to both branded and generic products, and Spurious/falsely-labelled/falsified/counterfeit pharmaceutical products may include products with the correct ingredients, with the wrong ingredients, without active ingredients, with an incorrect quantity of active ingredient or with fake packaging.

Cross-contamination: Contamination of a starting material, intermediate product or finished pharmaceutical product with another starting material or product during production, storage and transportation.

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

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.

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 Spurious/falsely-labelled/falsified/counterfeit, 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 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.

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.

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 medicines 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.

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 Spurious/falsely-labelled/falsified/counterfeit. 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 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.

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.

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

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

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

5. GENERAL GUIDANCE AND PRINCIPLES

5.1 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.

5.2 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.

5.3 The principles of GDP should also be adhered to in the case of pharmaceutical products that are donated.

5.4 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.

5.5 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 Spurious/falsely-labelled/falsified/counterfeit pharmaceutical products.

6. ROLE AND RESPONSIBILITIES OF DISTRIBUTORS

6.1 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 EFMHACA 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.

6.2 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.

6.3 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.

6.4 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.

6.5 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.

6.6 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.

7. QUALITY MANAGEMENT

7.1 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.

7.2 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.

7.3 The quality system should include provisions to ensure that the holder of the marketing authorization, entity identified on the label (if different from the manufacturer) and FMHACA, as well as other relevant competent authorities, would be informed immediately in a case of confirmed or suspected Spurious/falsely-labelled/falsified/counterfeiting of a pharmaceutical product. Such products should be stored in a secure, segregated area and clearly identified to prevent further distribution or sale.

7.4 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.

7.5 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.

7.6 Managerial and technical personnel must have the authority and resources needed to carry out their duties and to set up and maintain a quality system, as well as to identify and correct deviations from the established quality system.

7.7 The responsibilities placed on any one individual should not be so extensive as to present any risk to product quality.

7.8 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.

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

7.10 Where electronic commerce (e-commerce) is used, i.e., electronic means are used for any of the distribution steps, defined procedures and adequate systems should be in place to ensure traceability and confidence in the quality of the pharmaceutical products concerned. Electronic transactions (including those conducted via the Internet), relating to the distribution of pharmaceutical products, should be performed only by authorized persons or entities. Authorized procurement and release procedures for all administrative and technical operations performed should be in place to ensure that appropriate pharmaceutical products are sourced only from approved suppliers and distributed by approved entities.

7.11 Inspection, auditing and certification of compliance with a quality system (such as the applicable International Standardization Organization (ISO) series, or national or international guidelines) by external bodies are recommended. Such certification should not, however, be seen as a substitute for compliance with these GDP guidelines and the applicable principles of GMP relating to pharmaceutical products.

7.12 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 Spurious/falsely-labelled/falsified/counterfeit.

7.13 Distributors, 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.

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

7.15 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.

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

7.17 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.

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

7.19 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 SFFC products. 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.

8. PERSONNEL

8.1 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 SFFC and the avoidance of SFFC entering the supply chain. A record of all training, which includes details of subjects covered and participants trained, should be kept.

8.2 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.

8.3 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. EFMHACA regulations, directives, and standards relating to the qualifications and experience of personnel should be adhered to.

8.4 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.

8.5 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.

8.6 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.

8.7 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.

8.8 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 Spurious/falsely-labelled/falsified/counterfeiting of any product.

9. 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 EFMHACA guide to good storage practices for pharmaceuticals.

Storage Areas

9.1 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.

9.2 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 SFFC.

9.3 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.

9.4 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.

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

9.6 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.

9.7 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.

9.8 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.

9.9 Physical or other equivalent validated (e.g., electronic) segregation should be provided for the storage of rejected, expired, recalled or returned products and suspected Spurious/falsely-labelled/falsified/counterfeits. The products and the areas concerned should be appropriately identified.

9.10 Unless there is an appropriate alternative system to prevent the unintentional or unauthorized use of quarantined, rejected, returned, recalled or suspected SFFC

pharmaceutical products, separate storage areas should be assigned for their temporary storage until a decision as to their future has been made.

9.11 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.

9.12 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.

9.13 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.

Storage Conditions and Stock Control

9.14 Storage conditions for pharmaceutical products should be in compliance with the recommendations of the manufacturer.

9.15 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.

9.16 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.

9.17 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.

9.18 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

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

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

10.3 Where feasible, consideration should be given to adding technology, such as global positioning system (GPS) electronic tracking devices and engine-kill buttons to vehicles that would enhance the security of pharmaceutical products while in the vehicle.

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

10.5 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.

10.6 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.

10.7 Defective vehicles and equipment should not be used and should either be labeled as such or removed from service.

10.8 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.

10.9 Vehicles, containers and equipment should be kept clean and dry and free from accumulated waste. Organizations in charge of distribution must ensure that vehicles used are cleaned regularly.

10.10 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.

10.11 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.

10.12 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.

10.13 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.

10.14 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.

10.15 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 Spurious/falsely-labelled/falsified/counterfeit. Such goods should be securely packaged, clearly labeled, and accompanied by appropriate supporting documentation.

10.16 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.

11. SHIPMENT CONTAINERS AND CONTAINER LABELING

11.1 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.

11.2 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.

11.3 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.

11.4 Normally, internationally and/or nationally accepted abbreviations, names or codes should be used in the labeling of shipment containers.

11.5 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.

11.6 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. DISPATCH AND RECEIPT

12.1 Pharmaceutical products should only be sold and/or distributed to persons or entities that are authorized to acquire such products in accordance with the applicable national and

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

12.2 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.

12.3 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.

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

12.5 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 and names of contact persons;
- Complete business name, address (no acronyms), and status of the addressee (e.g., retail pharmacy, hospital or community clinic);
- Description of the products including, e.g., name, dosage form and strength (if applicable);
- Quantity of the products, i.e., number of containers and quantity per container (if applicable);
- Applicable transport and storage conditions;
- 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).

12.6 Records of dispatch should contain enough information to enable traceability of the pharmaceutical product. Such records should facilitate the recall of a batch of a product, if necessary, as well as the investigation of Spurious/falsely-labelled/falsified/counterfeit or potentially Spurious/falsely-labelled/falsified/counterfeit pharmaceutical products.

12.7 In addition, the assigned batch number and expiry date of pharmaceutical products should be recorded at the point of receipt to facilitate traceability.

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

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

12.10 Care should be taken to ensure that the volume of pharmaceutical products ordered does not exceed the capacity of storage facilities at the destination.

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

12.12 Pharmaceutical products should not be supplied or received after their expiry date, or so close to the expiry date that this date is likely to be reached before the products are used by the consumer. Incoming shipments should be examined to verify the integrity of the container/closure system and to ensure that tamper-evident packaging features and that labeling are intact.

12.13 When pharmaceutical products are being imported, they should follow appropriate FMHACA directives.

13. TRANSPORTATION AND PRODUCTS IN TRANSIT

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

13.2 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.

13.3 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.

13.4 Pharmaceutical products should be stored and transported in accordance with procedures such that:

- The identity of the product is not lost;
- The product does not contaminate and is not contaminated by other products;
- Adequate precautions are taken against spillage, breakage, misappropriation and theft; and
- Appropriate environmental conditions are maintained, e.g., using cold chain for thermos-labile products.

13.5 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.

13.6 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.

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

13.8 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.

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

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

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

13.12 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.

13.13 Drivers of vehicles should identify themselves and present appropriate documentation to demonstrate that they are authorized to transport the load.

13.14 Damage to containers and any other event or problem that occurs during transit must be recorded and reported to the relevant department, entity or authority, and investigated.

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

14. DOCUMENTATION

14.1 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.

14.2 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.

14.3 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.

14.4 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.

14.5 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.

14.6 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.

14.7 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.

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

14.9 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.

14.10 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.

14.11 Records relating to storage of pharmaceutical products should be kept and be readily available upon request in accordance with the EFMHACA Guidelines on Good Storage Practices for Pharmaceuticals.

14.12 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.

14.13 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.

14.14 Where the records are generated and kept in electronic form, backups should be maintained to prevent any accidental data loss.

15. RECALLS

15.1 There should be a system, which includes a written procedure, to effectively and promptly recall pharmaceutical products known or suspected to be defective or Spurious/falsely-labelled/falsified/counterfeit, 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.

15.2 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 Spurious/falsely-labelled/falsified/counterfeited product which is not easily distinguishable from the original product, the manufacturer of the original product and the relevant health authority should be informed.

15.3 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.

15.4 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.

15.5 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.

15.6 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 Spurious/falsely-labelled/falsified/counterfeit.

15.7 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).

15.8 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.

16. RETURNED PRODUCTS

16.1 A distributor should receive pharmaceutical product returns or exchanges pursuant to the terms and conditions of the agreement between the distributor and the recipient. Both distributors and recipients should be accountable for administering their returns process and ensuring that the aspects of this operation are secure and do not permit the entry of Spurious/falsely-labelled/falsified/counterfeit products.

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

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

16.4 Rejected pharmaceutical products and those returned to a distributor should be appropriately identified and handled in accordance with a procedure which involves at least:

- Physical segregation of such pharmaceutical products in quarantine in a dedicated area; or
- Other equivalent (e.g., electronic) segregation.

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

16.6 Provision should be made for the appropriate and safe transport of rejected pharmaceutical products prior to their disposal.

16.7 Destruction of pharmaceutical products should be done in accordance with waste management and disposal directive of EFMHACA.

16.8 Records of all returned, rejected and/or destroyed pharmaceutical products should be kept for a predetermined period.

17. SPURIOUS/FALSELY-LABELLED/FALSIFIED/COUNTERFEIT PHARMACEUTICAL PRODUCT

17.1 Spurious/falsely-labelled/falsified/counterfeit pharmaceutical products found in the distribution chain should be kept apart from other pharmaceutical products to avoid any confusion. They should be clearly labeled as not for sale and national regulatory authorities and the holder of the marketing authorization for the original product should be informed immediately.

17.2 The sale and distribution of a suspected Spurious/falsely-labelled/falsified/counterfeit pharmaceutical product should be suspended and EFMHACA should be notified without delay. Upon confirmation of the product being Spurious/falsely-labelled/falsified/counterfeit, a formal decision should be made on its disposal, ensuring that it does not re-enter the market, and that decision should be recorded.

18. SELF-INSPECTION

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

18.2 Self-inspections should be conducted in an independent and detailed way by a designated, competent person.

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

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FOOD, MEDICINE AND HEALTH CARE ADMINISTRATION AND CONTROL AUTHORITY OF ETHIOPIA (EFMHACA)

PART III
PHARMACEUTICAL PRODUCTS RECALL GUIDELINES

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ACRONYMS

CAPA	Corrective Action And Preventive Action
EFMHACA	Food, Medicine and Healthcare Administration and Control Authority of Ethiopia
PQM	Promoting the Quality of Medicines Program
SOP	Standard Operating Procedure
USAID	United States Agency for International Development
USP	U. S. Pharmacopeial Convention

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 (EFMHACA).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 Food, Medicine and Healthcare Administration and Control Authority (EFMHACA) of Ethiopia.

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 EFMHACA. For any Licensee that has failed to comply with those conditions, EFMHACA may revoke or suspend the license for a period of time that it believes appropriate.

The role of EFMHACA 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. EFMHACA 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 EFMHACA.

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.

Definitions

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.

Pharmaceutical product: Any substance, or combination of substances, manufactured, sold, supplied or offered for sale or supply for use in the diagnosis, treatment, restoration, mitigation, alleviation or prevention of a disease or its symptoms.

Recall : Recall means firm's removal of marketed pharmaceutical product that EFMHACA considers to be unsafe ,inefficacious and poor quality .Recall doesn't not include market withdrawal or returned products.

Steps of Recall Procedure

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

1. **Receipt of Pharmaceutical Product Problem Report**
   Notification to EFMHACA (see also Pharmaceutical Product Problem Report Form, Part 1 (Appendix I)

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

3. **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.
4. **Communication**
   Letters and press release (if required) are dispatched to relevant firms for notifying on the recall. See the Recall Reply Format (Appendix II).
5. **Progress of Recall and Report**
   Progress reports and a final report are submitted EFMHACA. See the Final Report Form (Appendix III).
6. **Evaluation of the Recall**
   The effectiveness of the recall is monitored by EFMHACA.

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 EFMHACA. 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 EFMHACA (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 EFMHACA 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 EFMHACA 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 EFMHACA 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 EFMHACA *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.

Initiation of Recall and Information required for Assessment

When the Licensee decides to initiate a recall on a pharmaceutical product, it must notify EFMHACA 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 EFMHACA, the Licensee and other organization involved in distribution must submit the information outlined below. Contact information for the concerned directorate of EFMHACA is provided by EFMHACA on the reporting form. The Licensee should submit the available information to EFMHACA 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 EFMHACA 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.

Role and Responsibilities of Stakeholders

1. EFMHACA can initiate a recall or approve a recall initiated by a manufacturer, importer or distributor. Although EFMHACA 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 EFMHACA or a pharmaceutical manufacturer or importer, etc.
   - Should also report pharmaceutical quality problems to EFMHACA

3. Pharmaceutical manufacturers, importers and organization involved in the distribution
   - Should have their own recall Standard Operating Procedures (SOPs)
   - Should notify EFMHACA of recall initiation.
   - Should conduct an effective recall in consultation with EFMHACA.
   - Should assess the effectiveness of the recall and report any recall they made to EFMHACA.
4. Wholesalers
   - Should cooperate in any recall conducted by EFMHACA, 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 EFMHACA, manufacturers, importers and distributors.
6. Medicine retail outlets
   - Should cooperate in the implementation of any recall initiated by EFMHACA, manufacturers, importers and distributors.
7. Healthcare professionals
   - Should cooperate in the implementation recall initiated by EFMHACA, manufacturers, importers and distributors.

Assessment of Recall

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 EFMHACA. The recall should be completed by the date directed by EFMHACA.

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 EFMHACA; and EFMHACA 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.

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. EFMHACA determines the classification and may seek expert advice when the nature of the hazard or its significance is not clear.

Level of Recall

As it does with the classification of a recall, EFMHACA 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

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 letterhead, 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. EFMHACA 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 EFMHACA.

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.

Responsibilities of Licensees

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.

Records

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 EFMHACA when a recall is implemented.

Recall Procedure

As mentioned in the above sections, the Licensee should prepare standard operating procedures for recall actions that are consistent with these Guidelines and that are applicable to their own operations. All top management personnel should be familiar with their responsibilities in connection with the procedures and with the records system for pharmaceutical products.

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 EFMHACA. 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.

Recall

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 EFMHACA.

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

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 EFMHACA. All Class I recalls should be completed within the time frame found suitable for the case as agreed by EFMHACA.

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 EFMHACA 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 EFMHACA 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 EFMHACA 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 EFMHACA 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.

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.

EFMHACA 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, EFMHACA 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 EFMHACA 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 EFMHACA 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.

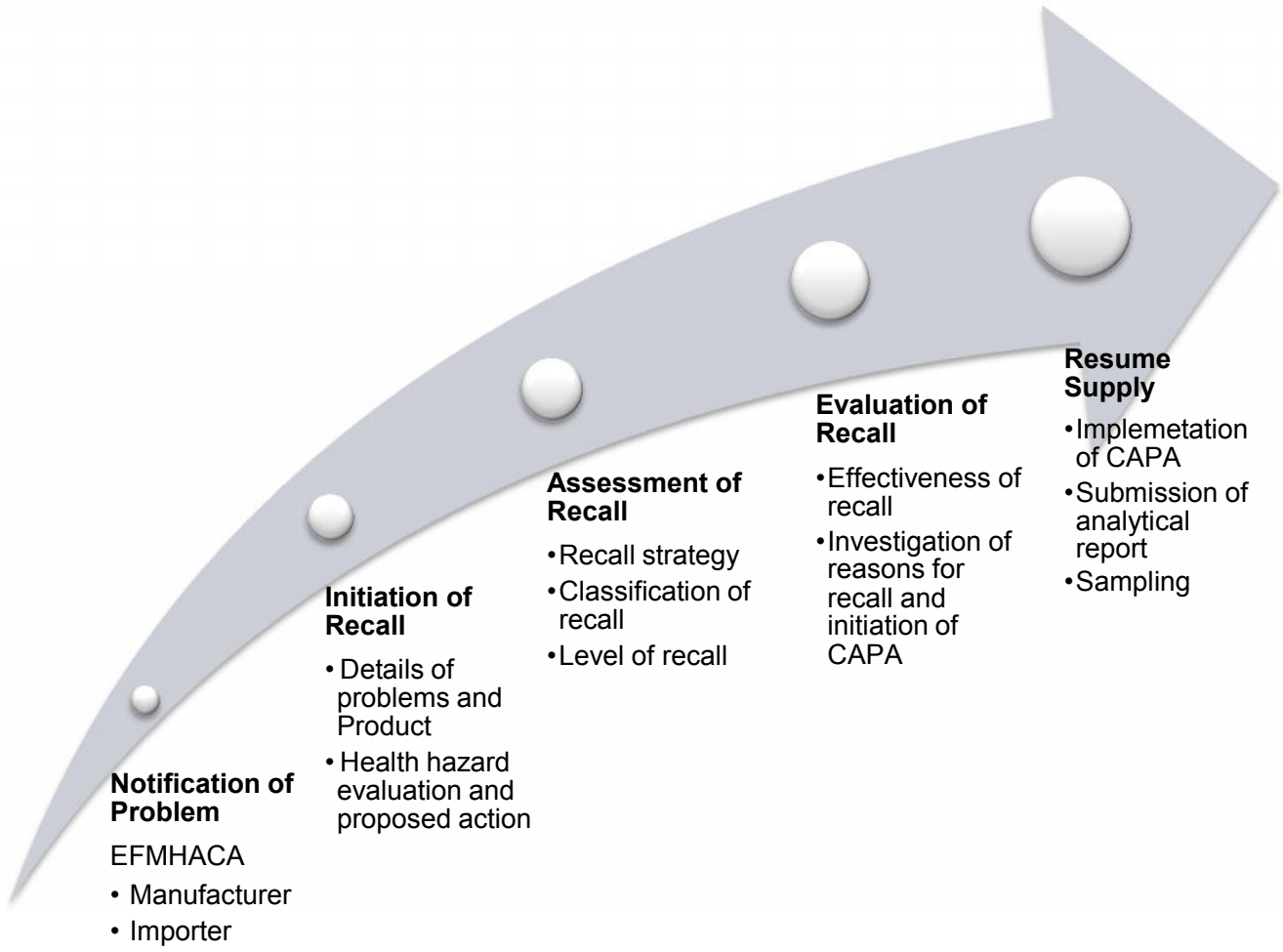
Submission of Analytical Report

After implementing the CAPA and subsequently manufacturing or importing a new batch of the product, the Licensee shall submit an analytical report(s) to EFMHACA of the new batch as tested by an external ISO accredited or WHO prequalified laboratory as a proof of product quality. EFMHACA 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 EFMHACA 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 EFMHACA 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 EFMHACA 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 EFMHACA.

Flow Chart of the Recall Process



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 EFMAHCA.

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 EFMHACA 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 EFMHACA pharmacist immediately by telephone and followed by facsimile or email.

The Licensee should submit the available information to EFMHACA 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 EFMHACA 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 EFMHACA pharmacist.

Contact information for the designated EFMHACA pharmacist:

Tel: _____

Email: _____
Fax Number: _____

Use a separate form for each pharmaceutical product reported.

Pharmaceutical Product Problem Report Form (Part I)

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

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

Name of Reporter_____ Position _____

Contact Number _____ Date _____

Signature of the reporter _____

Recall Notification Form (Part II)

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

Name of reporter _____ Position _____

Contact Number ……. Date _____

Signature of the reporter _____

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 _____

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 _____

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 EFMHACA 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.