



**NATIONAL PHARMACEUTICAL REGULATORY DIVISION
MINISTRY OF HEALTH MALAYSIA**

THIRD EDITION, 1 JANUARY 2018

GUIDELINE ON GOOD DISTRIBUTION PRACTICE

DRAFT CONFIDENTIAL

TABLE OF CONTENTS

INTRODUCTION.....	3
CHAPTER 1: QUALITY MANAGEMENT.....	4
CHAPTER 2: PERSONNEL.....	6
CHAPTER 3: PREMISES AND EQUIPMENTS.....	7
CHAPTER 4: STOCK HANDLING AND STOCK CONTROL.....	11
CHAPTER 5: TRANSPORTATION.....	15
CHAPTER 6: PRODUCTS/COSMETICS COMPLAINTS.....	18
CHAPTER 7: PRODUCTS/COSMETICS RECALL.....	19
CHAPTER 8: COUNTERFEIT PRODUCTS/ COSMETICS.....	22
CHAPTER 9: OUTSOURCED ACTIVITIES.....	23
CHAPTER 10: SELF-INSPECTION.....	23
CHAPTER 11: MANAGEMENT OF RECORDS AND DOCUMENTATION.....	25
ANNEX 1: MANAGEMENT OF TIME AND TEMPERATURE SENSITIVE PRODUCTS.....	28
ANNEX 2: SPECIFIC PROVISIONS FOR BROKERS.....	31
ANNEX 3: GENERAL POINTS TO CONSIDER FOR AUDITEE.....	32
GLOSSARY OF TERMS.....	33
REFERENCES.....	36

INTRODUCTION

Distribution is an important activity in the integrated supply-chain management. With the globalisation of the pharmaceutical industry, various individuals and organisations from locations around the world are generally responsible for handling, storage and distribution of such products. Therefore it is important to have adequate control over the entire supply chain from manufacture to delivery to the patient or end user. This guideline lays down the appropriate principles for those involved in the supply chain in conducting their activities while ensuring the maintenance of high standards of quality assurance and integrity of the distribution processes. Not all of the principles described will be relevant to every situation as it is recognised not all the principles are applicable to certain companies or environment. The principles should be adapted to meet individual company's needs where necessary. Alternative practices to those set out in the guideline that achieve an equivalent or better outcome can be adopted by companies provided that such alternative practices can be shown or demonstrated to achieve an outcome that is equivalent to or better than the provisions in the guideline. When the distribution chain is interrupted by manufacturing steps such as repackaging or relabelling, the principles of Good Manufacturing Practice (GMP) should be applied to these processes.

This guideline is applicable to all organisations and individuals involved in any aspect of the storage and distribution of products/cosmetics including but not limited to the following:

- Manufacturers of active pharmaceutical ingredients, drug products, radiopharmaceuticals, packaging materials, dietary supplements, biological and biotechnological products, and cell and gene therapy products.
- Packaging operations by the manufacturer or a designated contractor for the Product Registration Holder.
- Repackaging operations in which the products/cosmetics may be owned by an organisation other than the primary manufacturer.
- Pharmacies including but not limited to retail, compounding and hospital.
- Importers and exporters.
- Wholesale distributors.
- Distribution organisations involved in road, rail, sea and/or air services.
- Third-party and fourth-party logistics providers, brokers and freight forwarders.
- Health care professionals storing products prior to dispensing or administering to patients.

This guideline also requires that products classified as dangerous drugs, scheduled poisons and psychotropic substances, under the Dangerous Drugs Act 1952 (Revised 1980), Poisons Act 1952 (Revised 1989), Poisons (Psychotropic Substances) Regulations 1989 and the Control of Drugs and Cosmetics Regulations 1984 (Revised 2009), are stored and distributed in accordance with the requirements of the respective Acts and Regulations.

CHAPTER 1: QUALITY MANAGEMENT

PRINCIPLE

A quality system setting out responsibilities, processes and risk management principles in relation to the activities of importation, procurement, storage, transportation and distribution of products/cosmetics should be maintained. All relevant activities should be clearly defined in procedures and systemically reviewed. All critical steps of the processes and significant changes should be justified and where relevant validated. The quality system is the responsibility of the organisation's management and requires their leadership and active participation and should be supported by personnel commitment.

QUALITY SYSTEM

- 1.1 Quality management system should include an appropriate organisational structure, procedures, processes and resources; and systematic actions necessary to ensure adequate confidence that a product/cosmetic will satisfy given requirements for quality. Totality of these actions is termed 'Quality System'. The Quality System should be fully documented and its effectiveness monitored.
- 1.2 The quality system should ensure that:
 - i. Products/Cosmetics are procured, held, supplied, imported, exported and distributed in a way that is compliant with the requirements of GDP;
 - ii. Management responsibilities are clearly defined;
 - iii. Products/Cosmetics are delivered to the right recipients within a satisfactory time period;
 - iv. Records are made contemporaneously (simultaneously/ at same time);
 - v. Deviations from established procedures are documented and investigated;
 - vi. Appropriate corrective and preventive actions (commonly known as CAPA) are taken to correct deviations and prevent them in line with the principles of quality risk management.
- 1.3 Quality system should also foster a safe, transparent and secure distribution system by establishing measures to ensure that products/cosmetics have a form of documentation that can be used to permit traceability of the products/cosmetics throughout distribution channels from the manufacturers, manufacturer's agents, wholesalers, importers, distributors and brokers to the retailers.
- 1.4 The quality system should extend to the control and review of any outsourced activities related to the procurement, holding, supply, import, storage, transport, distribution or export of products/cosmetics. These processes should include:

- i. Assessing the suitability and competence of the Contract Acceptor to carry out the activity and checking authorisation status, if required;
 - ii. Defining the responsibilities and communication processes for the quality related activities of the parties involved;
 - iii. Monitoring and review of the performance of the Contract Acceptor, and the identification and implementation of any required improvements on a regular basis.
- 1.5 Authorised procurement and release procedures for all administrative and technical operations performed should be in place, to ensure that appropriate products/cosmetics are sourced from approved suppliers and distributed by approved entities. The approval should come from the competent authority of the individual country where the legal entity is registered. There should be a written procedure in place to ensure and document traceability of the products/cosmetics received and distributed.
- 1.6 Where electronic commerce (e-commerce) is used, defined procedures and adequate systems should be in place to ensure traceability and confidence in the quality of products/cosmetics. The provisions should guarantee the same degree of products/cosmetics safety as it can be achieved in non e-commerce.
- 1.7 Inspection and certification of compliance with a quality system (such as International Organisation for Standardisation (ISO) series, or national or international guidelines) by external bodies is recommended. Such certification, however, should not be seen as a substitute for compliance with the guideline.

CHAPTER 2: PERSONNEL

PRINCIPLE

There must be sufficient competent personnel to carry out all the assigned tasks. Individual responsibilities should be clearly understood by the personnel and be recorded.

GENERAL

- 2.1 The company must have an organisation chart. Personnel in responsible positions should have specific duties recorded in written job descriptions and adequate authority to carry out their responsibilities. Their duties may be delegated to designated deputies of a satisfactory qualification level. There should be no gaps or unexplained overlaps in the responsibilities of those personnel concerned with the application of GDP.
- 2.2 Besides the basic training on the theory and practice of GDP, newly recruited personnel should receive training appropriate to the duties assigned to them. Continuous training should also be given, and its practical effectiveness should be periodically assessed. Training program should be available and approved. Training records should be kept.
- 2.3 Personnel should receive training specific to their tasks given (e.g. evaluation of goods upon receiving, evaluation of complaints about damage during process, return to saleable stock of returned used goods, products which require stringent handling conditions such as hazardous products, radioactive materials, products presenting special risks of abuse (including narcotics and psychotropic substances), fragile products and time and temperature sensitive products (TTSP).
- 2.4 In addition, training should include aspects of product identification and avoidance of falsified products/cosmetics entering the supply chain.
- 2.5 Appropriate procedures relating to personnel hygiene and for appropriate clothing of personnel, relevant to the activities being carried out, should be established and observed. Personnel should be trained accordingly. Clothing should be adequate for the activities to be performed.

CHAPTER 3: PREMISES AND EQUIPMENT

PRINCIPLE

Premise and equipment must be suitable and adequate as to ensure proper loading, unloading and storage, protection from contamination and distribution of products/cosmetics. In particular, the premises should be clean, dry and maintained within acceptable temperature limits.

PREMISES

- 3.1 Premises should protect products/cosmetics from contamination and deterioration by light, moisture and temperature.
- 3.2 Premises should have sufficient security to prevent unauthorised access and misappropriation of the goods. Visitors should be accompanied.
- 3.3 Premise must have a permanent address and be located at a site approved by the local authority and/or other related Acts or Regulations which must be adhered to by the licensee.
- 3.4 Where premises are not directly operated by the company, a written contract should be in place. The contracted premises should have a separate authorisation of distribution.
- 3.5 The receiving and dispatched areas should be appropriately designed. They should protect products/cosmetics from weather. The receiving areas should be designed and equipped to allow cleaning of the containers of incoming products/cosmetics, if necessary, before storage.
- 3.6 There should be adequate storage areas to allow orderly and segregated storage of various categories of products/cosmetics: those in quarantine and released, rejected, returned or recalled. These designated storage areas should be clearly marked and the access to the quarantine, rejected, returned or recalled area should be restricted to authorised personnel. Any system (e.g. Computerised and bar coding system) replacing the physical separation should be given equivalent assurance segregation and restriction in accessibility.
- 3.7 The requirements under the regulations governing the storage of scheduled poisons, dangerous drugs and psychotropic substances must be taken into consideration.
- 3.8 Rest, wash and refreshment rooms for personnel should be adequately separated from the storage area. The presence of food, drink, smoking materials should be prohibited in the storage areas.

- 3.9 Products/cosmetics should be stored separately from non-medicinal products (medical devices, etc).
- 3.10 The premises should be designed or adapted to ensure that the required storage conditions are maintained. They should be suitably secure and of sufficient capacity to allow safe storage and handling of products/cosmetics. Storage areas should be provided with adequate lighting and ventilation to enable all operations to be carried out accurately and safely.
- 3.11 Storage facilities should be clean and free from accumulated waste and dust. A written sanitation programme should be available indicating the frequency of cleaning and the methods used to clean the premises and storage areas. Cleaning record should be maintained. There should be appropriate procedures for the cleaning up if any spillage to ensure complete removal of any risk of contamination.
- 3.12 Products/cosmetics should be stored off the floor and suitably spaced to permit cleaning and inspection. Pallet should be well maintained and kept in a good state of cleanliness.
- 3.13 The storage area should be designed and equipped to prevent the entry of insects, rodents and other pests/animals. There should also be a written programme for pest control and appropriate record should be kept.
- 3.14 Appropriate and suitable storage conditions should be provided for hazardous, sensitive and dangerous products such as combustible liquids and solids, pressurised gases, highly toxic substances and radioactive materials/products subject to local legislations and appropriate security and safety measures.
- 3.15 Printed packaging materials are considered a critical conformity of the products/cosmetics and special attention should be paid to the proper and secure storage of these materials.
- 3.16 Storage conditions for products/cosmetics should be in compliance with the instruction on the label. The storage area should be equipped with recorders or devices that will continuously monitor the storage conditions and record the relevant readings such as maximum and minimum temperature and humidity of the day. Appropriate actions on the premises, equipment and/or products/cosmetics should be taken when the storage conditions are not met and these actions should be recorded.
- 3.17 The records and devices for monitoring the storage conditions should be located in areas that are most likely to show fluctuations and/or the hottest and coldest locations

where appropriate. This measuring equipment should be calibrated for the required operating range at regular intervals. Such calibrations records should be maintained.

- 3.18 An initial temperature mapping exercise should be carried out on the storage area before use, under representative conditions. Temperature monitoring equipment should be located according to the results of the mapping exercise, ensuring that monitoring devices are positioned in the areas that experience the extremes of fluctuations. The mapping exercise should be repeated for significant changes according to the results of a risk assessment exercise. Relevant document and records should be retained. Where current regulations state a period for retention of records, this should be followed.

EQUIPMENT

- 3.19 All equipment impacting on storage and distribution of products/cosmetics should be designed, located, maintained and cleaned to a standard which suits its intended purpose. Planned maintenance should be in place for key equipment vital to the functionality of the operation.
- 3.20 Adequate procedures and records of operations, repair, maintenance and calibration activities for key equipment should be in place including cleaning and safety precautions. Key equipment would include for example cold rooms/stores, monitored intruder alarm and access control system, refrigerators, thermohygrometers or other temperature and humidity recording devices, air handling units and any equipment used in conjunction with the onward supply chain.
- 3.21 Equipment used to distribute or transport products/cosmetics should be suitable for their use and appropriately equipped to prevent exposure of the products/cosmetics to conditions that could affect their stability and packaging integrity, and prevent contamination of any kind.
- 3.22 Where non-dedicated equipment is used, procedures must be in place to ensure that the quality of the products/cosmetics will not be compromised.
- 3.23 Equipment used for monitoring conditions within vehicles and containers, e.g. temperature and humidity, should be calibrated, at regular intervals.
- 3.24 For time and temperature sensitive products (TTSP), qualified equipment (e.g. thermal packaging, temperature-controlled containers or temperature controlled vehicles) should be used to ensure correct transport conditions are maintained between the manufacturer, wholesale distributor and end user. The scope and extent of such

qualification and/or validation should be determined using a documented risk assessment approach. Validation and qualifications reports should be prepared summarising the results obtained and commenting on any observed deviations. Deviations should be documented and further actions decided to correct deviations and avoid their occurrence. Evidence of satisfactory validation and acceptance of a process or a piece of equipment should be produced and approved by appropriate personnel.

- 3.25 Before a computerised system is brought into use, it should be demonstrated through appropriate validation or verification studies, that the system is capable of achieving the desired results accurately, consistently and reproducibly. A written, detailed descriptions of the system should be available (including diagram where appropriate). This should be kept up to date. The documents should describe principles, objectives, security measures, system scope, main features, how the computerised system is used and the ways it interacts with other system.
- 3.26 Data should only be entered into the computerised system or amended by persons authorised to do so. Data should be secured by physical or electronic means and protected against accidental or unauthorised modifications. Stored data should be checked periodically for accessibility. Data should be protected by backing up at regular intervals.
- 3.27 Procedures to be followed if the system fails or breaks down should be defined. This should include systems for the restoration of data.

CHAPTER 4: STOCK HANDLING AND STOCK CONTROL

PRINCIPLE

All actions taken should ensure that the identity of the products/cosmetics is not lost and the distribution of products/cosmetics is performed according to the information on the outer packaging. The risk of falsified products/cosmetics entering the legal supply chain should be eliminated/minimised. All supplies of products/cosmetics must only be purchased from approved suppliers or companies that are authorised by the authorities. Where products/cosmetics are obtained from another wholesaler, the receiving wholesaler must verify that the supplier complies with the principles and guidelines of good distribution practices and that they hold a valid licence issued by the authority. All products/cosmetics purchased from suppliers and distributed in the intended market by company must be appropriately authorised by the authority. All key operations should be fully described in the quality system in appropriate documentation.

RECEIVING

- 4.1 Upon receipt, each incoming delivery should be checked against the relevant documentation and physically verified by label description, type and quantity, against the relevant purchase order information including certificate of analysis and originated from approved suppliers. The consignment should be examined for uniformity and if necessary should be subdivided according to the supplier's lot numbers should the delivery comprise of more than one batch.
- 4.2 All containers should be carefully inspected for tampering, contamination and damage and if necessary the suspected container or the entire delivery should be quarantined or set aside for further investigation. Records should be retained for each delivery.
- 4.3 Delivery order should include the description of the goods, quality (if applicable), quantity, supplier details, supplier's batch number, the date of receipt and assigned batch number. Where current regulations state a period for retention of records, this should be followed.
- 4.4 Products/cosmetics should remain in quarantine status until a given written release/rejected statement is issued by the authorised personnel.
- 4.5 Products subject to specific storage requirements (e.g. narcotics, time and temperature sensitive products (TTSP) should be immediately identified and stored in accordance with the written procedure.

STOCK ROTATION AND CONTROL

- 4.6 Periodic stock reconciliation should be performed comparing the actual and recorded products/cosmetics quantity. All significant stock discrepancies should be subjected to investigation to check against inadvertent mix-ups and wrong issues of stock.
- 4.7 Issues should normally observe the principle of stock rotation (FIFO/FEFO) especially where expiry dated products/cosmetics are concerned.
- 4.8 Products/cosmetics with broken seals, damaged packaging or suspected of possible contamination must not be sold or supplied.
- 4.9 All stocks should be checked regularly for expired products/cosmetics. All due precautions should be observed to preclude issuance of expired products/cosmetics.
- 4.10 All labels and containers of products/cosmetics should not be altered, tampered or changed. Acts and regulations relating to labels and containers should be adhered to at all times.
- 4.11 Products/cosmetics in cartons/bulk packs should be adequately labelled with at least the product name, batch number and expiry date or retest date.
- 4.12 Repacking (including relabelling) of products/cosmetics must be carried out only by company who hold an appropriate licence or approval from authority, unless the activities are exempted from these requirements.

RETURNED AND REJECTED

- 4.13 All returned and rejected products/cosmetics should be placed in quarantine and be clearly marked as such. They should be stored separately in restricted area.
- 4.14 Returned products/cosmetics must be handled according to a written, risk based process taking into account the product concerned, any specific storage requirements and the time elapsed since the product/cosmetic was originally dispatched. Returns should be conducted in accordance with national legislation, and contractual arrangements between the parties. A record/ list of returned goods must be maintained.

- 4.15 The fate of returned and rejected products/cosmetics should be determined after sufficient evaluation by trained and competent person authorised to do so.
- 4.16 Provision should be made for the appropriate and safe transport and storage of returned or rejected products/cosmetics in accordance with the relevant storage and other requirements.
- 4.17 Products/cosmetics returned to saleable stock should be placed such that the stock rotation system operates effectively.
- 4.18 Stolen products/cosmetics that have been recovered cannot be returned to saleable stock and sold to end user.
- 4.19 All action taken should be approved and recorded.
- 4.20 Any counterfeit products/cosmetics found in the distribution network should be physically segregated from other products/cosmetics to avoid any confusion. They should be clearly labelled as 'Not For Sale' or with other similar phrases/words. The regulatory authority and the holder of the marketing authorisation of the original product should be informed immediately.
- 4.21 Records of returned products/cosmetics should be maintained. For each return, documentation should include:
- Name and address of the consignee returning the products/cosmetics.
 - Name or designation of products/cosmetics, batch number and quantity returned
 - Reasons for return
 - Use or disposal of the returned products/cosmetics and record of the assessment performed.

DISTRIBUTION

- 4.22 Controls should be in place to ensure the correct product/cosmetic is picked. The product should have an appropriate remaining shelf life when it is picked.
- 4.23 The allocation of shipping materials should be carried out only after receipt of a sales order. Requirements for distribution procedures should be established depending on the nature of the products/cosmetics, and after taking into account any special precautions to be observed.
- 4.24 Import and export activities should be conducted in accordance with national legislation and with international guidelines or standards when appropriate. This is

also the case if the wholesalers or importers are holding products in a free trade zone. Wholesalers should take the appropriate measures in order to prevent products/cosmetics not authorised for the internal market and intended for export from reaching the internal market.

- 4.25 Deliveries should be made only to wholesale dealers or persons who are authorised to supply the products/cosmetics.
- 4.26 A written procedure on the delivery of the products/cosmetics to end users should be available.
- 4.27 A system should be in place by which the distribution of each batch of products/cosmetics can be readily identified to permit its recall.
- 4.28 For all suppliers, a document (eg. Deliver Order) must be enclosed stating the date, name of products/cosmetics, batch number, quantity supplied, name and address of supplier, name and delivery address of the consignee (actual physical storage premise, if different) and applicable transport and storage conditions. Records should be kept so that the actual location of products/cosmetics can be known.

DISPOSAL

- 4.29 Products/cosmetics intended for destruction should be appropriately identified, segregated accordingly and handled in accordance with written procedure.
- 4.30 Destruction of products/cosmetics should be carried out in accordance with the national legislative and regulatory requirements and with due consideration to protect the environment.
- 4.31 Disposal records should be maintained for a defined period.

CHAPTER 5: TRANSPORTATION

PRINCIPLE

It is the responsibility of all manufacturers, importers and wholesalers of products/cosmetics to protect their products against breakage, adulteration, theft and to ensure that temperature conditions are maintained within acceptable limits during transport.

Regardless of the mode of transport, it should be possible to demonstrate that the products/cosmetics have not been exposed to conditions that may compromise their quality and integrity. A risk-based approach should be utilized when planning transportation.

GENERAL

- 5.1 Vehicles used to distribute or transport products/cosmetics should be suitable for their use and appropriately equipped to prevent exposure of the products/cosmetics to conditions that could affect their stability and packaging integrity, and prevent contamination of any kind.
- 5.2 Dedicated vehicles should be used, where possible, when handling products /cosmetics. Where non-dedicated vehicles are used, procedures must be in place to ensure that the quality of the products/cosmetics will not be compromised. Appropriate cleaning should be performed, checked and recorded.
- 5.3 There should be procedures in place for the operation and maintenance of all vehicles involved in the distribution process, including cleaning and safety precautions. There should also be written program for pest control. Cleaning and fumigation agents should not have an adverse effect on products/ cosmetics quality.
- 5.4 Risk assessment of delivery routes should be used to determine where temperature controls are required. Equipment used for monitoring conditions within vehicles and containers, e.g. temperature and humidity, should be calibrated, at regular intervals.
- 5.5 Vehicles and containers should be of sufficient capacity to allow orderly storage of the various categories of products/cosmetics during transportation.
- 5.6 Measures should be in place to prevent unauthorised persons from entering and/or tampering with vehicles, as well as to prevent the theft or misappropriation thereof.

- 5.7 Products/cosmetics should be secured in such a manner to prevent or provide evidence of unauthorised access. Shipments should be secured and include the appropriate documentation to ensure that identification and verification of compliance with regulatory requirements is facilitated at ocean ports, truck borders, airports, custom warehouses and third party logistic providers.
- 5.8 Products/cosmetics should be stored and transported in accordance with procedures in such a way that: the identity of the products/cosmetics is not lost; the products/cosmetics does not contaminate and is not contaminated by other products/cosmetics; adequate precautions are taken against spillage, breakage, misappropriation and theft; and temperature and relative humidity conditions are maintained accordingly.
- 5.9 Measures should be established to ensure that products/cosmetics have a form of documentation that can be used to permit traceability of the products/cosmetics throughout the distribution activity.
- 5.10 Written procedures should be in place for investigating and dealing with any excursions of storage requirements, e.g. temperature excursions.
- 5.11 Transportation and storage of products comprising highly active and radioactive materials, other dangerous drugs and substances presenting special risks of abuse, fire or explosion (e.g. combustible liquids, solids and pressurized gases) should be stored in safe, dedicated and secure areas and transported in safe, dedicated and secure containers and vehicles. In addition, applicable international agreements and national legislation should be complied with.
- 5.12 Packaging materials and transportation containers should be of suitable design to prevent damage of products/cosmetics during transport. If there are seal control programs, such programs should be in place and managed properly (e.g. seals are issued and tracked in a sequential manner, seals are intact and numbers verified during transit and upon receipt).
- 5.13 Containers should bear labels providing sufficient information on handling and storage requirements and precautions to ensure that the products/cosmetics are properly handled and secured at all times. The containers should enable identification of the contents of the containers and the source.
- 5.14 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.

- 5.15 Where possible, mechanisms should be available to allow for the segregation during transit of rejected, recalled and returned products/cosmetics as well as those suspected to be counterfeits. Where feasible, such goods must be securely packaged, clearly labelled, and be accompanied by appropriate supporting documentation.
- 5.16 Where transportation is performed by a third party, the contract should be in place covering the requirements of Chapter 9. Transportation providers should be made aware by manufacturers, manufacturer's agents, wholesalers, importers, distributors and brokers of the relevant transport conditions applicable to the consignment. Where the transportation route includes unloading and reloading or transit storage at a transportation hub, particular attention should be paid to temperature monitoring, cleanliness and the security of any intermediate storage facilities.
- 5.17 Company is responsible to ensure the competency of the transportation provider elected. Besides that, it is the responsibility of the company to ensure that the elected transportation provider reports the incident or deviation, if any, which occurred during the transportation or distribution process.

CHAPTER 6: PRODUCTS/COSMETICS COMPLAINTS

PRINCIPLE

All complaints must be recorded and handled carefully according to written procedures. Records should be made available to competent authority. An assessment of returned products/cosmetics should be performed by designated personnel before any approval for resale.

GENERAL

- 6.1 Complaints should be recorded with all the original details. A distinction should be made between complaints related to the quality of the products/cosmetics and those related to distribution. In the event of a complaint about the quality of the products/cosmetics and a potential product/cosmetic defect, the manufacturer and/or product registration holder of the product/cosmetic should be informed without delay. Any products/cosmetics distribution complaint should be thoroughly investigated to identify the origin of or the reason for the complaint.
- 6.2 Procedures shall be developed within the company for the handling of all written and oral complaints regarding a possible product/cosmetic defect. There should also be a record for each individual product/cosmetic complaint.
- 6.3 The procedure shall ensure that the complaints received are investigated and followed through and that all corrective actions are taken to prevent repeated complaints. The investigation should also cover distribution condition and the condition under which the product/cosmetic is used. The complainant shall be provided with a response after the completion of the investigation.
- 6.4 A person should be designated/appointed to handle complaints. This person must have the authority to initiate investigations and to decide on the measures to be taken. The contact details of the designated/appointed person should be included in the procedure.
- 6.5 If a product/cosmetic defect is discovered or suspected in a batch, consideration should be given to determine whether other batches are also affected.

CHAPTER 7: PRODUCTS/COSMETICS RECALLS

PRINCIPLE

The Control of Drugs and Cosmetics Regulations 1984, requires every licensed manufacturer, importer and wholesaler to have a procedure (Product Recall Procedure), which sets out in a step-wise manner the various actions to be taken to ensure the prompt recall of defective products/cosmetics. Such procedures should be reviewed regularly and updated.

DEFINITION

Product recall is a process taken by the manufacturer, importer and wholesaler to remove or withdraw a particular products and/or cosmetics from all links of distribution.

The removal or withdrawal may be due to critical quality defects discovered or serious adverse drug reactions reported which might cause health risks to users of the products/cosmetics.

DECISION FOR RECALL

The decision for recall shall be made when there is or may caused potential risk to the user of the products/cosmetics by reason of faulty production or on medical grounds:

- Voluntarily undertaken by the manufacturers and distributors.
- As directed by the Director of Pharmaceutical Services, Ministry of Health.

Unless the Director of Pharmaceutical Services, Ministry of Health has already specified the degree and level of a particular products/cosmetics recall, the degree and level will be decided by the company's Product Recall Committee based on risks involved.

The Product Recall Committee shall comprise of personnel who are responsible for the execution and coordination of recall. The persons responsible shall handle all aspects of the recalls with the appropriate degree of urgency.

DEGREE AND LEVEL OF RECALL

The following criteria are used to classify the degree and level of recall.

DEGREE OF RECALL

The degree of recall is classified according to the severity of quality defects and adverse reactions of the products/cosmetics.

Degree I – Products/Cosmetics with major health risks that might caused serious injuries or death. Should be under an embargo within 24 hours.

Degree II – Products/Cosmetics with minor health risks or are substandard. Should be under an embargo within 72 hours.

Degree III – Products/Cosmetics with other reasons for recall. Should be under an embargo within 30 days or as specified.

LEVEL OF RECALL

The level of recall depends on the nature of problem, extent of the product/cosmetic's distribution and degree of hazard involved.

Level A: To all consumers (end users)

Level B: To all points of sales (e.g. Hospitals, Pharmacies, Clinics, Specialists Centres)

Level C: To all sub-distributors (wholesalers)

GENERAL

- 7.1 A person or committee should be designated for the co-ordination and execution of all product recalls. The contact details of the designated person or committee should be included in the procedure.
- 7.2 In the event of a product/cosmetic recall, all end users to whom the products/cosmetics have been distributed shall be informed with the appropriate degree of urgency. The notification of recall should include:
- The name of the products/cosmetics, its strength (if necessary) and pack size.
 - The products/cosmetics batch number, the nature of the defect.
 - Whether the recall should be carried out at the consumer level (end users), all points of sale or sub-distributors (wholesalers and retail) level.
 - The action to be taken.
 - The urgency of the action (with reasons, indication of health risk, as appropriate).
- 7.3 The local regulatory authority should be informed of all products/cosmetics recalls. If the products/cosmetics are exported, the overseas counterparts and/or regulatory authorities must be informed of the recall.
- 7.4 Where products/cosmetics recall affects a particular batch, consideration should also be given to determine whether other batches are also affected.

- 7.5 The storage conditions applicable to products/cosmetics which are subjected to recall should be maintained during storage and transit until a decision has been made regarding the products/cosmetics.
- 7.6 The progress of recall process should be recorded for a final report including reconciliation of the recalled products/cosmetics and a final report of the executed products/cosmetics recall will be forwarded to the local regulatory authority.

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CHAPTER 8: COUNTERFEIT PRODUCTS/COSMETICS

PRINCIPLE

Any counterfeit products/cosmetics found in the distribution network should be physically segregated from other products/cosmetics to avoid any confusion. They should be clearly labelled. All relevant activities in relation to such products/cosmetics should be documented and records retained. The sale and distribution of suspected counterfeit products/cosmetics should be suspended immediately. A consistent approach by all partners in the supply chain is required in order to be successful in the fight against falsified products/cosmetics.

GENERAL

- 8.1 The regulatory authority and the product registration holder of the original products/cosmetics should be informed immediately. A procedure should be in place to this effect. It should be recorded with all the original details and investigated.
- 8.2 Upon confirmation as counterfeit products/cosmetics, a formal decision should be taken on removal of such products/cosmetics from the market, ensuring that it does not re-enter the supply chain, including retention of any samples necessary for public health, regulatory, or legal needs and arrangements for its disposal. All related decisions should be appropriately documented.

CHAPTER 9: OUTSOURCED ACTIVITIES

PRINCIPLE

Any activities performed, referenced in the GDP guideline and delegated to another party should be correctly defined, agreed and controlled in order to avoid misunderstandings which could affect the integrity of the products/cosmetics. There must be a written contract between the Contract Giver and the Contract Acceptor which clearly established the duties of each party.

GENERAL

- 9.1 The Contract Giver is responsible for assessing the competency of the Contract Acceptor to successfully carry out the work required and for ensuring by means of the contract and through audits that the principles and guidelines of GDP are followed. Audits toward Contract Acceptor by the Contract Giver should be permitted at any time.
- 9.2 The Contract Acceptor should have adequate premises and equipment, procedures, knowledge, experience and competent personnel to carry out the work ordered by the Contract Giver.
- 9.3 The Contract Acceptor should not pass to a third party any of the work entrusted to him under the contract without the Contract Giver's prior evaluation and approval of the arrangements and an audit of the third party by the Contract Giver or the Contract Acceptor. Arrangements made between the Contract Acceptor and any third party should ensure that the wholesale distribution information is made available in the same way as between the original Contract Giver and Contract Acceptor.
- 9.4 Depending on the nature of activities performed, the Contract Acceptor should understand that he might subject to inspection by the regulatory authority.

CHAPTER 10: SELF-INSPECTION

PRINCIPLE

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

GENERAL

- 10.1 Self-inspections should be conducted covering all aspects of GDP and compliance with the regulations, guidelines and procedures within a defined time frame.
- 10.2 Self-inspections should be conducted in an independent and detailed way by a designated, competent person, according to an approved written procedure.
- 10.3 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 corrective actions taken and recorded.

CHAPTER 11: MANAGEMENT OF RECORDS AND DOCUMENTATION

PRINCIPLE

Policies and procedures should be in place to ensure:

- All records are kept in accordance with legislative requirements.
- All records are maintained in accordance with the general requirements of this guideline and other relevant guideline by the national regulatory authority.
- Prevent errors from verbal communication and permits the tracking of relevant operations during the receipt, storage and distribution of products/cosmetics.

Management of Documentation

11.1 Documentation comprises all written procedures, instructions, contracts, records and data. It may be in electronic or paper form. All documents should be approved, signed and dated by the appropriate authorised persons and not be changed without authorisation.

11.2 Documents should be:

- Clear, concise, comprehensible and readily available to those that need to use them;
- Numbered, dated, have a title, name and position of the person responsible for the documents;
- Include detailed instructions on the subject and a date for review.

Management of Records

11.3 Accurate record of all receipts and sales transactions must be kept.

11.4 Records should be made at the time each operation is taken in such a way that all significant activities or events are traceable. Records should be clear and readily available. The retention of documentation relating to distribution of products/cosmetics should comply with national requirements.

11.5 If records are computerised, only authorised persons should be able to enter or modify data in the computer. Access should be restricted by passwords or other means. Users should have a unique identifier (User ID) for their personal and sole use so that activities can subsequently be traced to the responsible individual.

11.6 Records electronically stored should be protected by back-up transfer on paper or other means, at regular intervals. It is particularly important that the data, including

audit trail, are readily available throughout the period of retention. Back-up data should be stored as long as necessary at a separate and secure location.

- 11.7 In accordance with the requirements specified by the regulatory authority, manufacturers/importers must record the usage of each hologram label used. In the case of any hologram labeling activity that is done by third party, the delivery/distribution record of hologram usage must be kept/recorded for traceability purpose.
- 11.8 Where applicable, full Material Safety Data Sheet (MSDS) and Certificate of Analysis (CoA) of products/cosmetics should be available.
- 11.9 All relevant legal records and documentations should comply to the current legislations referring to:
- a. Poisons Act 1952 and its regulations
 - b. Sale of Drugs Act 1952
 - c. Control of Drugs and Cosmetics Regulations 1984
 - d. Dangerous Drugs Act 1952
 - e. Dangerous Drugs Regulations 1952

11.10 **Wholesale Records**

*Records of Transactions (Regulation 27),
Control of Drugs and Cosmetics Regulations 1984:*

Applicable for all registered products/cosmetics other than scheduled poisons, psychotropic substances and dangerous drugs.

Entries to be made in Records of Transactions (For Licensed Wholesaler).

These records should include:-

- Date of sale/supply
- Name and address of supplier/purchaser
- Name, quantity and strength of products/cosmetics received/sold
- Registration Reference of the products/cosmetics
- Batch No.
- Invoice No./Delivery Order No.

11.11 Importation Records

*Records of Transactions (Regulation 27),
Control of Drugs and Cosmetics Regulations 1984:*

Applicable to all registered products/cosmetics other than scheduled poisons, psychotropic substances and dangerous drugs.

Entries to be made in Records of Transactions (For Licensed Importer).

These records should include:-

- Date of Importation
- Name and address of supplier/purchaser
- Name, quantity and strength of products/cosmetics imported/supplied
- Invoice No./Bill Landing No./Airway Bill No.
- Date of Sale/Supply
- Name and address of purchaser
- Registration reference of the products/cosmetics
- Batch No.
- Invoice No./Delivery No.

ANNEX 1: MANAGEMENT OF TIME AND TEMPERATURE SENSITIVE PRODUCTS (TTSP)

PRINCIPLE

Policies and procedures should be available to ensure that the activities of receipt, storage and distribution are done without compromising on the quality, efficacy, safety and integrity of time and temperature sensitive products (TTSP) according to the manufacturer's recommended conditions as per the approved product's label by the authority as well as the product stability data.

GENERAL

1. List of products including the cold chain storage temperature specifications should be provided for reference to personnel who handle the receipt of goods.
2. Regular and appropriate training should be provided for all personnel (including drivers) involved in the handling of TTSP to ensure the quality of TTSP are maintained. The training should also cover on applicable pharmaceutical legislations and regulations; SOPs and safety issues and response to emergencies. Training records and effectiveness checks on training provided should be available upon request.
3. Net storage capacity of the storage facilities should be sufficient to accommodate peak TTSP stock levels under correct temperature conditions and in a manner which enables efficient and correct stock management operations to take place.
4. TTSP storage facilities should be qualified prior to prevail that it is capable of storing the product in accordance with the specifications given situation. Qualification and validation records must be kept and TTSP storage facilities must be able to operate at all time in accordance to the qualifying conditions.
5. Household-style unit refrigerators and freezers are only acceptable if they have been independently tested and found to comply with the temperature control requirements of a recognized standard for pharmaceutical refrigerators or freezers.
6. Controlled or hazardous TTSP should be stored in dedicated, separated and securely locked facilities/areas that comply fully with all legislative and regulatory requirements.
7. Cold room, freezer room, refrigerator and freezer must be fitted with an alarm system to alert personnel if any occurrence of temperature beyond specifications. Action and warning limits should be established. Periodic testing program on the alarm system should be established to ensure the alarm system is functioning.

8. Alternative power systems should be established to ensure temperature remained and the temperature/humidity detector will continue functioning in the event of power failure. Periodic testing program on alternative power systems should be established to ensure that it works. Alternative plan to provide alternative areas where storage temperature equivalent should be provided if no alternative power systems can be provided.
9. Calibration and temperature monitoring functions of all equipment, including alarms and other related equipment, must be inspected at least annually.
10. Periodic maintenance program for all temperature controlled rooms, cold rooms, freezer rooms, refrigerators and freezers must be established and implemented.
11. Verification upon receipt of products should be done to ensure there are no signs of tampering and non-conformance (such as deviation of temperature profile from the manufacturer's recommendation as per the approved product's label by the authority, physical damage to products, packaging materials, etc.).
12. All TTSP (e.g. rejected, quarantined) must be stored under the storage conditions stated on the label other than the product which will be disposed off. If the storage temperature is found to have deviated from the storage specifications, manufacturer for the products should be contacted to confirm the suitability of the use of products and the decision recorded.
13. Maximum and minimum temperature and humidity (if needed) for all temperature controlled rooms, cold rooms, freezer rooms, refrigerators and freezers must be monitored and recorded continuously using temperature and humidity monitoring devices.
14. Suitability of locations for placing temperature sensors in all temperature controlled rooms, cold rooms, freezer rooms, refrigerators and freezers used for storage of TTSP should be subjected to temperature mapping study. Mapping studies should be conducted in accordance with written procedures and storage conditions determined before operation.
15. Container systems used for delivery of TTSP should be fully qualified to show that it is 'fit for purpose' and capable of maintaining the temperature profile defined for each product during transportation/distribution, can minimize product degradation due to temperature sensitivity and can meet the product stability profile requirements stated

by the pharmaceutical manufacturer. Documented evidence of such assurance and compliance should be demonstrated and available upon request.

16. Packaging operations for TTSP should be verified in accordance with written procedures. Packaging for TTSP should be mapped and continuously monitored.
17. There should be a system in place to control the reuse of temperature protection components (e.g. ice/water blankets, water/gel packs, phase change materials, insulated packaging, etc.) to ensure that incomplete components are not used in error.
18. Necessary precaution steps should be implemented when using dry ice during transportation in order to avoid a direct contact with the product and consequently caused coagulation of products.
19. TTSP should be clearly labelled and identifiable from other products in the same delivery. In cases where TTSP are to be air freighted, the package(s) should be labelled according to the International Air Transport Association (IATA) regulations.
20. Procedures must be implemented to handle the returned products and also the products that have been stored under out of the specified storage condition during the reception, storage and distribution of products.
21. TTSP should be transported under validated conditions to ensure that the relevant temperature range is maintained according to the directions on the label of the products. In addition, simulation studies can be conducted to validate the delivery conditions, taking into account the possibility of the worst situation.
22. Refrigerated vehicles or containers to transport TTSP should be mapped and continuously monitored.
23. Delivery route planning for TTSP should be created to prevent the risk of exposure to the products beyond the control of the ambient temperature. TTSP should be clearly identified from other items in the same distribution activities.
24. Products labelled "Keep Frozen" should be transported in such a manner to ensure that it remains frozen.

ANNEX 2: SPECIFIC PROVISIONS FOR BROKERS

This section is applicable or relevant to brokers, agents, traders, dealers or distributors. A 'broker' is a person involved in activities in relation to the sale or purchase of medicinal products, except for wholesale distribution, that do not include physical handling and that consist of negotiating independently and on behalf of another legal or natural person. It is also applicable to those brokers that may trade and/or take possession, distribute or store an API or intermediate.

They must have a permanent address and contact details. They must notify the regulatory authority of any changes to those details without unnecessary delay. All requirements in this guideline also apply to brokers.

1. The quality system of a broker should be defined in writing, approved and kept up to date. It should set out responsibilities, processes and risk management in relation to their activities.
2. Any companies involved in the brokering activities should have personnel trained particularly in the issues concerning falsified products, handling of complaints and recall. All relevant activities should be clearly defined in procedures and systemically reviewed and record accordingly.
3. Brokers that deal in API or intermediate should maintain complete traceability of products/materials that are being distributed. Such documents include name and address of the original manufacturer, purchase orders, transportation documentation, manufacturer's batch number, transportation and distribution records as well as original Certificate of Analysis from the manufacturer.
4. Original Certificates of Analysis issued by the manufacturer or authenticated copies of the original Certificates of Analysis for each batch of intermediates or APIs should be provided to the customers upon request.
5. The general provisions on documentation in Chapter 11 apply.

ANNEX 3: GENERAL POINTS TO CONSIDER FOR AUDITEE

General Points to Consider	
<p>Personnel</p> <ul style="list-style-type: none"> • Organization chart • Job Description • Training <ul style="list-style-type: none"> ○ Program/ Procedure ○ Records ○ Evaluation • Hygiene, clothing <ul style="list-style-type: none"> ○ Program/ Procedures <p>Premises and Facilities</p> <ul style="list-style-type: none"> • Adequate storage area with segregations • Appropriate for the products • Lights/ ventilation <ul style="list-style-type: none"> ○ Cleaning procedure/ records • License with Local Authority • Program & Records <ul style="list-style-type: none"> ○ Pest control ○ Sanitation • Temperature & Humidity monitoring <ul style="list-style-type: none"> ○ Calibrated devices ○ Records ○ Range suitable for stored products • Maintenance of facilities/ utilities • Any contract warehouse(s) <ul style="list-style-type: none"> ○ Approval available for the use of the warehouse <p>Stock Handling & Stock control</p> <ul style="list-style-type: none"> • FIFO/FEFO concept • Appropriate type of checks conducted • Control on reject, returned, expired stock • Records/ documents -traceability • Procedures <ul style="list-style-type: none"> ○ Receiving ○ Delivery ○ Stock handling ○ Stock Reconciliation • Updated inventory records • Record & Control of expiry dates • Record & Control of hologram usage • CoA (for imported products) <p>Disposal</p> <ul style="list-style-type: none"> • Procedures • Records 	<p>Transportation</p> <ul style="list-style-type: none"> • Transporting document • Suitability of vehicle used • Temperature Mapping • Monitoring of Storage Conditions during transportation or simulation study • Procedures & Records <ul style="list-style-type: none"> ○ Operation ○ Maintenance ○ Pest control <p>Product Complaints</p> <ul style="list-style-type: none"> • Procedures and Records • System for Response, Investigation & follow-up <p>Product recall</p> <ul style="list-style-type: none"> • Procedures and Records <p>Counterfeit products</p> <ul style="list-style-type: none"> • Procedures • Records <p>Self inspection</p> <ul style="list-style-type: none"> • Program-plan, frequency ,scope • SOP and Records <p>Outsourced Activities</p> <ul style="list-style-type: none"> • Responsibilities and requirements of Contract Giver and Contract Acceptor clearly established • Contracts <p>Time & Temperature Sensitive Products</p> <ul style="list-style-type: none"> • List of products • Labels/ means to identify products • Procedure – Receiving, Storage, Distribution, Packing & Independent Check, Packaging, Returned Products • Training programme and records • Temperature and Humidity Monitoring • Qualification and validation of equipments • Alarm System for Temperature Excursion • Alternative power systems for cold room • Temperature mapping for vehicles/ storage facility or qualified/ validated containers • Monitoring of storage conditions during transportation or simulation study • Procedure for handling temperature excursion • Contracts • Calibration and maintenance

GLOSSARY OF TERMS

Term	Definition
Active Pharmaceutical Ingredient (API)	Any substance or mixture of substances intended to be used in the manufacture of a drug product and that when used in the production of a drug becomes an active ingredient of the drug product. Such substances are intended to furnish pharmacological activity or other direct effects in the diagnosis, cure, mitigation, treatment or prevention of diseases, or to affect the structure and function of the body.
Authorities	Refer to government bodies or agencies such as local authorities, state health department as well as Ministry of Natural Resources & Environment given lawful approval or recognition on particular responsibilities.
Counterfeit product or cosmetic	Product or cosmetic which is deliberately and fraudulently mislabeled with respect to identity and/or source. Counterfeiting can apply to both branded and generic products/cosmetics and may include products/cosmetics with the correct ingredients or with wrong ingredients, without active ingredients, with insufficient active ingredients or with fake packaging.
Consignment	The delivery batch of products/cosmetics supplied at one time in response to a particular request or order.
Contamination	The undesired introduction of impurities of a chemical or microbiological nature, or of foreign matter during manufacturing, sampling, packaging or repackaging, storage or transport.
Cosmetic	<p>Means:</p> <ol style="list-style-type: none"> <li data-bbox="532 1409 1385 1696">a. Any substance or preparation intended to be placed in contact with the various external parts of the human body (including epidermis, hair system, nails, lips and external genital organs) or with the teeth and mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfume them, changing their appearance or correcting body odours, protecting them or keeping them in good condition. <li data-bbox="532 1728 1385 1843">b. A cosmetic product currently notified in accordance with the provisions of the Sale of Drugs Act 1952 and the Control of Drugs and Cosmetics Regulations 1984.

Cross-contamination	Contamination of a material or product or cosmetic with another material or product or cosmetic.
Good Distribution Practice (GDP)	The measures that need to be considered in the storage, transportation and distribution of any registered product/notified cosmetic and such that the nature and quality intended is preserved when it reaches the consumer.
Intermediate (API Intermediate)	A material produced during the processing step of an API which must undergo further molecular change or purification before it becomes an API.
Labelling	The term 'labelling' designates all labels and other written, printed or graphic matter upon, or in, any package or wrapper in which it is enclosed, except any outer shipping container. A shipping container, unless such container is also essentially the immediate container or the outside of the consumer package, is exempt from labelling requirements.
Licence	Any licence issued under Regulation 12 of the Control of Drugs and Cosmetics Regulations 1984.
Manufacturer	Includes: <ul style="list-style-type: none"> a. the making or assembling of the products/cosmetics; b. the enclosing or packing of the product in any container in a form suitable for administration or application, and the labelling of the container; and c. the carrying out of any process in the course of any or the foregoing activities.
Manufacturer's Agent	Representatives or companies acting as agents empowered by the manufacturer to sell or solicit sales for the manufacturer's products in a defined territory.
Packaging material	Any material employed in the packaging of products/cosmetics, including any other 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.

Printed packaging material	Packaging material which is a imprinted with text or numbers or a combination of both.
Product	Means: <ul style="list-style-type: none"> a. a drug in a dosage unit or otherwise, for use wholly or mainly by being administered to one or more human beings or animals for medicinal purpose;or b. a drug to be used as an ingredient of a preparation for medicinal purpose. c. raw materials, starting materials, intermediates, excipients, packaging materials and labeling materials. d. Applicable to Active Pharmaceutical Ingredients (if applicable)
Return product/cosmetic	Products/cosmetics sent back from the end user to the supplier.
Storage	A term used to describe the safe keeping of products or cosmetic such as starting materials and finished products received from supplier, semi-finished products or cosmetics in process and finished products awaiting dispatch and products or cosmetics awaiting distribution to retailers and products or cosmetics (rejected, recalled and damaged) awaiting disposal.
Supplier	A person providing products or cosmetics on request. Supplier may be agents, brokers, distributors, manufacturers or traders.
Temperature	Room temperature: 15 - 25°C or up to 30°C depends on climatic condition Cool temperature: 8 - 15°C Cold temperature: 2 - 8°C Frozen temperature: ≥ -20°C
Wholesale	A sale to any person who intends to sell again and any sale by a licensed wholesaler.

REFERENCES

1. PIC/S Guide to Good Distribution Practice for Medicinal Products, PE-011-1, 1 June 2014
2. WHO Good Distribution Practices for Pharmaceutical Products. WHO Technical Report Series, No. 957, 2010.
3. Guidelines for Storage of Essential Medicines and other Health Commodities. USAID in collaboration with the World Health Organisation (WHO), 2003.

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