ZAMBIA MEDICINES REGULATORY AUTHORITY

Certificates, Permits & Licences

GOOD DISTRIBUTION PRACTICES GUIDELINES

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GLOSSARY

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

Agreement
Arrangement undertaken by and legally binding on parties.

Audit
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 medicines and allied substances processed in a single process or series of processes so that it is expected to be homogeneous.

Batch number
A distinctive combination of numbers or letters which uniquely identifies a batch.

Consignment
The quantity of medicines and allied substances 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 medicines and allied substances belonging to more than one batch.

Container
The material employed in the packaging of a medicines and allied substance. Containers include primary, secondary and transportation containers. Containers are referred to as primary if they are intended to be in direct contact with the product. Secondary containers are not intended to be in direct contact with the product.

Contamination
The introduction of impurities of a chemical or microbiological nature, or of foreign matter, into or on to a starting material, intermediate or medicines and allied substances during handling, production, sampling, packaging or repackaging, storage or transportation.

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

Counterfeit medicines and allied substances
A medicines and allied substances which is deliberately and fraudulently mislabeled with respect to identity or source. Counterfeiting can apply to both branded and generic

products, and counterfeit medicines and allied substances 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 medicines and allied substance with another starting material or product during production, storage and transportation.

Distribution
The procuring, purchasing, holding, storing, selling, supplying, importing, exporting, or movement of medicines and allied substances, with the exception of the dispensing or providing medicines and allied substances directly to a patient or his or her agent.

Distributor
A person engaged in one or more of the distribution activities as defined under distribution.

Expiry date
The date given on the individual container (usually on the label) of medicines and allied substance 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 or used before an identical stock item with a later expiry date is distributed 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 medicines and allied substances 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 counterfeits, unapproved, illegally imported, stolen, , substandard and falsified medicines and allied substances.

Good manufacturing practices (GMP)
That part of quality assurance which ensures that medicines and allied substances 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 pharmacists, prime concern at all times.

Good storage practices (GSP)
That part of quality assurance that ensures that the quality of medicines and allied substances is maintained by means of adequate control throughout the storage thereof.

Good trade and distribution practices (GTDP)
That part of quality assurance that ensures that the quality of medicines and allied substances 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
Partly processed product that must undergo further manufacturing steps before it becomes a bulk finished product.

Labelling
Process of identifying medicines and allied substances including the following information, as appropriate: name of the product; active ingredient(s), type and amount; batch number; expiry date; special storage conditions or handling precautions; directions for use, warnings and precautions; names and addresses of the manufacturer or the supplier.

Manufacture
All operations of purchase of materials and products, production, packaging, labelling, quality control, release, storage and distribution of medicines and allied substances, and the related controls.

Marketing authorisation
A legal document issued by the Zambia 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 International Non- proprietary Names (INN) or national generic names where they exist), the shelf-life and storage conditions, and packaging characteristics.
It specifies the information on which authorisation is based (for example "The product(s) must conform to all the details provided in your application and as modified in subsequent correspondence"). It also contains the product information approved for health professionals and the public, the sales category, the name and address of the

holder of the authorization, and the period of validity of the authorisation. Once a product has been given marketing authorization, it is included on a list of authorized products − the register − and is often said to be "registered" or to "have registration". Market authorization may occasionally also be referred to as a "licence" or "product licence".

Pharmaceutical waste means Obsolete, unwanted or expired medicines, herbal medicines, raw materials or allied substances including unwanted packaging materials

Product recall
A process for withdrawing or removing medicines and allied substances from the pharmaceutical distribution chain because of defects in the product, complaints of serious adverse reactions to the product or concerns that the product is or may be 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 medicines and allied substances 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 medicines and allied substances 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 medicine and allied substances, based on an appropriate statistical procedure, for a defined purpose, for example acceptance of consignments or batch release.

Shelf-life
The period of time during which a medicine and allied substance, 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 (for example

equipment operation, maintenance and cleaning, validation, cleaning of premises and environmental control, sampling and inspection).

Storage
The storing of medicines and allied substances up to the point of use.

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

Transit
The period during which medicines and allied substances 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 medicines and allied substances.

1. INTRODUCTION

Distribution is an important activity in the integrated supply-chain management of medicines and allied substances. 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 objective of these guidelines is to assist in ensuring the quality and identity of medicines and allied substances during all aspects of the distribution process. These aspects include, but are not limited to, procurement, purchasing, storage, distribution, transportation, repackaging, relabelling, documentation and record-keeping practices.

The storage, sale and distribution of medicines and allied substances 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 counterfeits 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 medicines and allied substances.

The nature of the risks involved is likely to be similar to that for risks encountered in the manufacturing environment, for example, mix-ups, adulteration, contamination and cross-contamination. When the distribution chain is interrupted by manufacturing steps such as repackaging and relabelling, the principles of good manufacturing practices (GMP) should be applied to these processes.

Counterfeit medicines and allied substances 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 medicines and allied substances provide an avenue for 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 medicines and allied substances is a particular concern. Only a joint approach including all parties involved in the supply chain can be successful in the fight against counterfeit medicines and allied substances and, therefore, all parties active in the market should take an active part in collaborative activities.

These guidelines are intended to be applicable to all persons and outlets involved in any aspect of the distribution of medicines and allied substances from the premises of the manufacturer of the product to the person dispensing or providing medicines and allied substances directly to a patient or his or her agent. This includes all parties involved in trade and distribution of medicines, pharmaceutical manufacturers, including the manufacturers of finished products, pharmaceutical wholesalers and government

institutions or departments involved in the distribution of medicines as well as other parties such as brokers, suppliers, distributors, logistics providers, traders, transport companies and forwarding agents and their employees.

To maintain the original quality of medicines and allied substances, every party active in the distribution chain has to comply with the applicable legislation and regulations. Every activity in the distribution of medicines and allied substances should be carried out according to the principles of GMP, Good Storage Practices (GSP) and Good Distribution Practices (GDP) as applicable.

These guidelines should be read together with other related applicable guidelines.

2. SCOPE OF THE DOCUMENT

This document lays down guidelines for the distribution of medicines and allied substances. These guidelines apply to products for human and veterinary use.

The document does not specifically cover GMP aspects of finished products in bulk, distribution of labels or packaging, as these aspects are considered to be covered by other guidelines.

These guidelines do not cover commercial relationships between parties involved in distribution of medicinal products nor questions of safety at work.

3. GENERAL PRINCIPLES

3.1 All parties involved in the distribution of medicines and allied substances have a responsibility to ensure that the quality of medicines and allied substances and the integrity of the distribution chain is 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.

3.2 The principles of GDP are applicable both to medicines and allied substances moving forward in the distribution chain from the manufacturer to the entity responsible for dispensing or providing medicines and allied substances to the patient and to products which are moving backwards in the chain, for example, as a result of the return or recall thereof.

3.3 The principles of GDP should also be adhered to in the case of medicines and allied substances which are donated.

3.4 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.

4. REGULATION OF THE DISTRIBUTION OF MEDICINES AND ALLIED SUBSTANCES

4.1 The distributor shall be a registered wholesale dealer and a holder of a Pharmaceutical Licence issued by the Authority.

4.2 Only persons or entities which are registered wholesale dealers and holders of a Pharmaceutical Licence issued by the Authority shall be entitled to import or export medicines and allied substances.

4.3 Distributors or their agents shall only distribute medicines and allied substances if a marketing authorization or similar authorization has been granted, which allows the use of those medicines and allied substances in the country.

4.4 Holders of an authorization to distribute medicines and allied substances shall obtain their supplies of medicines and allied substances only from persons or entities which are in possession of the marketing authorization to sell or supply such products to a distributor.

4.5 Distributors or their agents shall supply medicines and allied substances 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.

4.6 Distributors or their agents shall ensure that there are 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. Distributors should periodically audit such activities with regard to application of GDP.

4.7 If a distributor or his or her 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.

5. ORGANIZATION AND MANAGEMENT

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

5.2 Duties and responsibilities shall 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.

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

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

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

5.6 There shall 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 medicines and allied substances.

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

6. PERSONNEL

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

6.2 Key personnel involved in the distribution of medicines and allied substances shall have the ability and experience appropriate to their responsibility for ensuring that medicines and allied substances are distributed properly.

6.3 There shall be an adequate number of competent personnel involved in all stages of the distribution of medicines and allied substances in order to ensure that the quality of the product is maintained.

6.4 Personnel dealing with hazardous medicines and allied substances (such as highly active materials, radioactive materials, narcotics, and other hazardous, environmentally sensitive or dangerous medicines and allied substances, as well as products presenting special risks of abuse, fire or explosion) shall be given specific training.

6.5 Personnel involved in the distribution of medicines and allied substances shall wear garments suitable for the activities that they perform. Personnel dealing with hazardous medicines and allied substances, including products containing materials that are highly active, toxic, infectious or sensitizing, shall be provided with protective garments as necessary.

6.6 Appropriate procedures relating to personnel hygiene, relevant to the activities to be carried out, shall be established and observed. Such procedures shall cover health, hygiene and clothing of personnel.

6.7 Codes of practice and punitive procedures shall be in place to prevent and address situations where persons involved in the distribution of medicines and allied substances are suspected of, or found to be implicated in, any activities relating to the misappropriation, tampering, diversion or counterfeiting of any product.

7. QUALITY SYSTEM

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 shall 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 shall include provisions to ensure that the holder of the marketing authorization, entity identified on the label (if different from the manufacturer), the Authority, as well as other relevant competent authorities, would be informed immediately in a case of confirmed or suspected falsifying of a medicine or allied substance. Such products shall be stored in a secure, segregated area and clearly identified to prevent further distribution or sale.

7.4 Authorized procurement and release procedures for all administrative and technical operations performed shall be in place to ensure that appropriate medicines and allied substances are sourced only from approved suppliers and distributed by approved entities.

7.5 If measures to ensure the integrity of the medicines and allied substances in transit are in place, they shall be managed properly. For example, if seal control programmes 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 medicines and allied substances are suspected of being or are found to be counterfeit.

7.6 Distributors should from time to time conduct risk assessments to assess potential risks to the quality and integrity of medicines and allied substances. The quality system should be developed and implemented to address any potential risks identified. The quality system should be reviewed and revised periodically to address new risks identified during a risk assessment.

Traceability of medicines and allied substances

7.7 Distributors should ensure availability of procedures to ensure document traceability of products received and distributed, to facilitate product recall.

7.8 All parties involved in the supply chain should be identifiable and traceable.

7.9 Measures shall be in place to ensure that medicines and allied substances 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. Records including expiry dates and batch numbers may be part of a secure distribution documentation enabling traceability.

7.10 A suitable and, to the extent possible, internationally compatible product coding, identification system shall be in place and developed in collaboration with the various parties involved in the supply chain.

8. PREMISES, WAREHOUSING AND STORAGE

8.1 Good storage practices (GSP) are applicable in all circumstances where medicines and allied substances are stored and throughout the distribution process.

Storage areas

8.2 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.

8.3 Storage areas shall be of sufficient capacity to allow the orderly storage of the various categories of medicines and allied substances, namely commercial and non-commercial products, products in quarantine, and released, rejected, returned or recalled products as well as those suspected to be counterfeits.

8.4 Storage areas shall 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. Medicines and allied substances 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.

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

8.6 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.

8.7 Receiving and dispatch bays should protect medicines and allied substances from the weather. Receiving areas shall be designed and equipped to allow incoming containers of medicines and allied substances to be cleaned, if necessary, before storage.

8.8 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.

8.9 Physical or other equivalent validated (for example electronic) segregation shall be provided for the storage of rejected, expired, recalled or returned products and suspected counterfeits. The products and the areas concerned should be appropriately identified.

8.10 Unless there is an appropriate alternative system to prevent the unintentional or unauthorized use of quarantined, rejected, returned, recalled or suspected counterfeit medicines and allied substances, separate storage areas shall be assigned for their temporary storage until a decision as to their future has been made.

8.11 Radioactive materials, narcotics, other hazardous, sensitive or dangerous medicines and allied substances, as well as products presenting special risks of abuse, fire or explosion (for example. combustible or flammable liquids and solids and pressurized gases) shall be stored in a dedicated area(s) that is subject to appropriate additional safety and security measures.

8.12 Medicines and allied substances shall be handled and stored in such a manner as to prevent contamination, mix-ups and cross-contamination.

8.13 A system shall be in place to ensure that the medicines and allied substances due to expire first are sold 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.

8.14 Broken or damaged items shall be withdrawn from usable stock and stored separately.

8.15 Storage areas shall be provided with adequate lighting to enable all operations to be carried out accurately and safely.

Storage conditions and stock control

8.16 Storage conditions for medicines and allied substances shall be in compliance with the recommendations of the manufacturer.

8.17 Facilities shall be available for the storage of all medicines and allied substances under appropriate conditions (for example environmentally controlled when necessary). Records shall be maintained of these conditions if they are critical for the maintenance of the characteristics of the medicines and allied substances stored.

8.18 Records of temperature monitoring data shall be available for review. There shall be defined intervals for checking temperature. The equipment used for monitoring shall 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 medicines and allied substances plus one year. 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.

8.19 Equipment used for monitoring of storage conditions shall also be calibrated at defined intervals.

8.20 Periodic stock reconciliation shall be performed by comparing the actual and recorded stocks. This shall be done at defined intervals.

8.21 Stock discrepancies shall be investigated in accordance with a specified procedure to check that there have been no inadvertent mix ups, incorrect issues and receipts, thefts or misappropriations of medicines and allied substances. Documentation relating to the investigation should be kept for a predetermined period.

9. VEHICLES AND EQUIPMENT

9.1 Vehicles and equipment used to distribute, store or handle medicines and allied substances shall 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. Preferably containerized transport or equivalent should be used.

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

9.3 Where feasible, consideration shall be given to adding technology, such as global positioning system (GPS) electronic tracking devices and engine-kill buttons to vehicles, which would enhance the security of medicines and allied substances while in the vehicle.

9.4 Dedicated vehicles and equipment shall be used, where possible, when handling medicines and allied substances.

9.5 Where non-dedicated vehicles and equipment are used, procedures shall be in place to ensure that the quality of the medicines and allied substances will not be compromised. Appropriate cleaning should be performed, checked and recorded.

9.6 Procedures shall be in place to ensure that the integrity of the products is not compromised during transportation.

9.7 Where third-party carriers are used, distributors shall develop written agreements with carriers to ensure that appropriate measures are taken to safeguard medicines and allied substances, including maintaining appropriate documentation and records. Such agreements should be in line with national and regional regulatory requirements.

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

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

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

9.11 Vehicles, containers and equipment shall be kept free from rodents, vermin, birds and other pests. There shall be written programmes and records for such pest control. The cleaning and fumigation agents used shall not have any adverse effect on product quality.

9.12 Equipment chosen and used for the cleaning of vehicles shall not constitute a source of contamination.

9.13 Special attention shall be paid to the design, use, cleaning and maintenance of all equipment used for the handling of medicines and allied substances which are not in a protective shipping carton or case.

9.14 Where special storage conditions (for example temperature or relative humidity), different from, or limiting, the expected environmental conditions, are required during transportation, these shall be provided, checked, monitored and recorded. All monitoring records shall be kept for a minimum of the shelf-life of the product distributed plus one year. Records of monitoring data should be made available for inspection by the Authority.

9.15 Equipment used for monitoring conditions, for example temperature and humidity, within vehicles and containers shall be calibrated at regular intervals.

9.16 Vehicles and containers shall be of sufficient capacity to allow orderly storage of the various categories of medicines and allied substances during transportation.

9.17 Where possible, mechanisms should be available to allow for the segregation during transit of rejected, recalled and returned medicines and allied substances as well as those suspected of being counterfeits. Such goods shall be securely packaged, clearly labelled, and be accompanied by appropriate supporting documentation.

9.18 Measures shall be in place to prevent unauthorized persons from entering or tampering with vehicles or equipment, as well as to prevent the theft or misappropriation thereof.

10. SHIPMENT CONTAINERS AND CONTAINER LABELLING

10.1 Medicines and allied substances shall 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.

10.2 Shipping containers shall 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 shall enable identification of the container's contents and source.

10.3 The need for any special transport and storage conditions shall be stated on the shipment container label. If medicines and allied substances are intended for transfer to areas outside the control of the manufacturer's products management system, the name and address of the manufacturer, special transport conditions and any special legal requirements, including safety symbols, shall also be included on the container label.

10.4 Normally, internationally or nationally accepted abbreviations, names or codes shall be used in the labelling of shipment containers.

10.5 Special care shall be taken when using dry ice in shipment containers. In addition to safety issues it must be ensured that the medicines and allied substances do not come into contact with the dry ice, as it may have an adverse effect on the quality of the product.

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

11. DISPATCH AND RECEIPT

11.1 Medicines and allied substances shall only be sold or distributed to persons or entities that are authorized to acquire such products. Documentary proof of such authority must be obtained prior to the distribution of products to such persons or entities.

11.2 Prior to the dispatch of the medicines and allied substances, the supplier shall ensure that the person or entity, for example, the contract acceptor for transportation of the medicines and allied substances, is aware of the medicines and allied substances to be distributed and complies with the appropriate storage and transport conditions.

11.3 The dispatch and transportation of medicines and allied substances shall be undertaken only after the receipt of a valid delivery order or material replenishment plan, which should be documented.

11.4 Written procedures for the dispatch of medicines and allied substances shall be established. Such procedures should take into account the nature of the product as well as any special precautions to be observed. Medicines and allied substances under quarantine will require release for dispatch by the person responsible for quality.

11.5 Records for the dispatch of medicines and allied substances 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, physical address (no acronyms), and status of the addressee (for example retail pharmacy, hospital or community clinic);
- a description of the products including, for example name, dosage form and strength (if applicable);
- quantity of the products, i.e. number of containers and quantity per container (if applicable);
- applicable transport and storage conditions;
- a unique number to allow identification of the delivery order; and assigned batch number and expiry date (where not possible at dispatch, this information should at least be kept at receipt to facilitate traceability).

11.6 Records of dispatch shall contain enough information to enable traceability of the medicines and allied substances. Such records shall facilitate the recall of a batch of a product, if necessary, as well as the investigation of counterfeit or potentially counterfeit medicines and allied substances.

11.7 In addition, the assigned batch number and expiry date of medicines and allied substances shall be recorded at the point of receipt to facilitate traceability.

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

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

11.10 Care shall be taken to ensure that the volume of medicines and allied substances ordered does not exceed the capacity of storage facilities at the destination.

11.11 Vehicles and containers shall 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 shall be taken during loading and unloading of cartons to avoid damage.

11.12 Medicines and allied substances shall 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.

11.13 Incoming shipments shall be examined to verify the integrity of the container-closure system, ensure that tamper-evident packaging features are intact, and that labelling appears intact.

12. TRANSPORTATION AND PRODUCTS IN TRANSIT

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

12.2 Product shipments shall be secured and 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 medicines and allied substances.

12.3 The people responsible for the transportation of medicines and allied substances shall be informed about all relevant conditions for storage and transportation. These requirements should be adhered to throughout transportation and at any intermediate storage stages.

12.4 Medicines and allied substances 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.
- Appropriate environmental conditions are maintained, for example using cold chain for thermolabile products.

12.5 The required storage conditions for medicines and allied substances shall be maintained within acceptable limits during transportation. If a deviation has been

noticed during transportation by the person or entity responsible for transportation, this shall be reported to the distributor and recipient. In cases where the recipient notices the deviation, it shall be reported to the distributor. Where necessary, the manufacturer of the medicines and allied substances shall be contacted for information about appropriate steps to be taken.

12.6 Where special conditions are required during transportation that are different from or limit the given environmental conditions (for example temperature and humidity) these shall be provided by the manufacturer on the labels, monitored and recorded.

12.7 Written procedures shall be in place for investigating and dealing with any failure to comply with storage requirements, for example temperature deviations.

12.8 Transportation and storage of medicines and allied substances containing hazardous substances, such as toxic, radioactive material, and other dangerous medicines and allied substances presenting special risks of abuse, fire or explosion (example combustible or flammable liquids, solids and pressurized gases) shall 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 shall be met.

12.9 Products containing narcotics and other dependence-producing substances shall be transported in safe and secure containers and vehicles and be stored in safe and secure areas.

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

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

12.12 The interiors of vehicles and containers shall remain clean and dry while medicines and allied substances are in transit.

12.13 Packaging materials and shipment containers shall be of suitable design to prevent damage of medicines and allied substances during transport. Seal control programmes should be in place and managed properly.

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

12.15 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.

12.16 Medicines and allied substances in transit must be accompanied by the appropriate documentation.

13. DOCUMENTATION

13.1 Written instructions and records which document all activities relating to the distribution of medicines and allied substances, including all applicable receipts and issues (invoices) shall be available. Records shall be kept for seven years, unless otherwise specified in national or regional regulations.

13.2 Distributors shall keep records of all medicines and allied substances received. Records shall contain at least the following information:

- date;
- name of the medicines and allied substances;
- quantity received, or supplied; and
- name and address of the supplier.

13.3 Procedures shall 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.

13.4 Documents, and in particular instructions and procedures relating to any activity that could have an impact on the quality of medicines and allied substances, shall be designed, completed, reviewed and distributed with care.

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

13.6 All documents shall be completed in indelible ink, approved, signed (as required) and dated by an appropriate authorized person(s) and shall not be changed without the necessary authorization.

13.7 The nature, content and retention of documentation relating to the distribution of medicines and allied substances and any investigations conducted and action taken, shall comply with national legislative requirements. Where such requirements are not in place, the documents shall be retained for at least one year after the expiry date of the product concerned.

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

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

13.10 Documents shall be reviewed regularly and kept up to date. When a document has been revised, a system shall exist to prevent inadvertent use of the superceded version.

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

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

13.13 Procedures shall 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 on retention of the records.

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

14. REPACKAGING AND RELABELLING

14.1 Repackaging and relabeling of medicines and allied substances shall be limited, as these practices may represent a risk to the safety and security of the supply chain.

14.2 Where they do occur, they shall only be performed by entities appropriately authorized to do so and in accordance with GMP principles.

14.3 In the event of repackaging by companies other than the original manufacturer, these operations shall result in at least equivalent means of identification and authentication of the products.

14.4 Procedures shall be in place for the secure disposal of original packaging.

15. COMPLAINTS

15.1 There shall be a written procedure in place for the handling of complaints. A distinction shall be made between complaints about a product or its packaging and those relating to distribution. In the case of a complaint about the quality of a product or its packaging, the original manufacturer or marketing authorization holder shall be informed as soon as possible.

15.2 All complaints and other information concerning potentially defective and potentially counterfeit medicines and allied substances shall be reviewed carefully according to written procedures describing the action to be taken, including the need to consider a recall where appropriate.

15.3 Any complaint concerning a material defect shall be recorded and thoroughly investigated to identify the origin or reason for the complaint (for example repackaging procedure or original manufacturing process).

15.4 If a defect relating to medicines and allied substances is discovered or suspected, consideration shall be given to whether other batches of the product shall also be checked.

15.5 Where necessary, appropriate follow-up action shall be taken after investigation and evaluation of the complaint. There shall be a system in place to ensure that the complaint, the response received from the original product manufacturer, or the results of the investigation of the complaint, are shared with all the relevant parties.

15.6 Product quality problems or suspected cases of counterfeit products shall be documented and the information shared with the appropriate national or regional regulatory authorities.

16. RECALLS

16.1 There shall be a system, which includes a written procedure, to effectively and promptly recall medicines and allied substances known or suspected to be defective or counterfeit, with a designated person(s) responsible for recalls. The system shall comply with the guidance issued by the Authority. This procedure shall be checked regularly and updated as necessary.

16.2 The original manufacturer or marketing authorization holder shall be informed in the event of a recall. Where a recall is instituted by an entity other than the original manufacturer or marketing authorization holder, consultation with the original manufacturer or marketing authorization holder shall, where possible, take place

before the recall is instituted. Information on a recall shall be shared with the Authority. If a recall of the original product is necessary because of a counterfeited product which is not easily distinguishable from the original product, the manufacturer of the original product and the Authority shall be informed.

16.3 The effectiveness of the arrangements for recalls shall be evaluated at regular intervals. All recalled medicines and allied substances shall be stored in a secure, segregated area pending appropriate action.

16.4 Recalled medicines and allied substances shall be segregated during transit and clearly labelled as recalled products. Where segregation in transit is not possible, such goods must be securely packaged, clearly labelled, and be accompanied by appropriate documentation.

16.5 The particular storage conditions applicable to medicines and allied substances which is subject to recall shall be maintained during storage and transit until such time as a decision has been made regarding the fate of the product in question.

16.6 All customers and competent authorities of all countries to which a given medicine and allied substance may have been distributed shall be informed promptly of any intention to recall the product because it is, or is suspected to be, defective or counterfeit.

16.7 All records shall be readily available to the designated person(s) responsible for recalls. These records shall contain sufficient information on medicines and allied substances supplied to customers (including exported products).

16.8 The progress of a recall process shall be recorded and a final report issued, which includes a reconciliation between delivered and recovered quantities of products.

16.9 When necessary emergency recall procedures shall be implemented.

17. RETURNED PRODUCTS

17.1 A distributor shall receive medicines and allied substances returns or exchanges pursuant to the terms and conditions of the agreement between the distributor and the recipient. Both distributors and recipients shall be accountable for administering their returns process and ensuring that the aspects of this operation are secure and do not permit the entry of counterfeit products.

17.2 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, shall all be taken into account in this assessment. Where any doubt arises over the quality of medicines and allied substances, it shall not be considered suitable for reissue or reuse.

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

17.4 Rejected medicines and allied substances and those returned to a distributor shall be appropriately identified and handled in accordance with a procedure which involves at least:

- the physical segregation of such medicines and allied substances in quarantine in a dedicated area; or
- equivalent (for example electronic) segregation.

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

17.6 Provision shall be made for the appropriate and safe transport of rejected medicines and allied substances prior to their disposal.

17.7 Destruction of medicines and allied substances shall be done in accordance with international, national and local requirements regarding disposal of such products, and with due consideration to protection of the environment.

17.8 Records of all returned, rejected or destroyed medicines and allied substances shall be kept for a predetermined period.

18. DISPOSAL OF PHARMACEUTICAL WASTE

18.1 Disposal of pharmaceutical waste shall be done in accordance with the current local guidelines on disposal of medicines and allied substances.

19. FALSIFIED AND SUBSTANDARD MEDICINES AND ALLIED SUBSTANCES

19.1 Falsified and substandard medicines and allied substances found in the distribution chain shall be kept apart from other medicines and allied substances to avoid any confusion. They shall be clearly labelled as not for sale and national regulatory authorities and the holder of the marketing authorization for the original product shall be informed immediately.

19.2 The sale and distribution of a suspected counterfeit medicines and allied substances shall be suspended and the national regulatory authority notified without delay.

19.3 Upon confirmation of the product being counterfeit a formal decision shall be taken on its disposal, ensuring that it does not re-enter the market, and the decision recorded.

20. IMPORTATION

20.1 At the port of entry, consignments of medicines and allied substances shall be stored under suitable conditions for as short a time as possible.

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

20.3 Where necessary, persons with pharmaceutical training shall be involved with the customs procedures or shall be readily contactable.

20.4 The products being imported should have Marketing Authorization issued by the Authority.

21. CONTRACT ACTIVITIES

21.1 Any activity relating to the distribution of medicines and allied substances which are delegated to another person or entity shall be performed by parties appropriately authorized for that function and in accordance with the terms of a written contract.

21.2 The contract shall define the responsibilities of each party including observance of the principles of GDP and relevant warranty clauses. It shall also include responsibilities of the contractor for measures to avoid the entry of falsified medicines and allied substances into the distribution chain, such as by suitable training programmes.

21.3 All contract accepters shall comply with the requirements in these guidelines.

21.4 Subcontracting may be permissible, under certain conditions and subject to the written approval of the contract giver; however, the subcontractors shall be authorized for the function.

22.5 Contract accepters shall be audited periodically.

22. SELF-INSPECTION

22.1 The quality system shall include self-inspections. Self-inspection of the various distribution activities at a site may be divided into several individual self-inspections of limited scope. However, the self-inspection programme should ensure that all of the significant distribution activities at the site are covered annually. Self-inspections shall be conducted to monitor implementation and compliance with the principles of GDP and, if necessary, to trigger corrective and preventive measures.

22.2 Self-inspections shall be conducted in an independent and detailed way by designated competent person(s).

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