MCAZ Medicines Control Authority of Zimbabwe

ZIMBABWE GUIDELINES FOR GOOD WHOLESALING PRACTICE OF MEDICINAL PRODUCTS

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1.0 APPLICATION

These guidelines apply to all persons, whether real or legal, that deal in the storage and distribution of medicinal products from the manufacturer of medicinal products to the person dispensing or providing medicines directly to the patient.

2.0 PURPOSE

Storage and distribution are important activities in the supply chain management of medicinal products. Medicinal products are subject to various risks at different stages of the supply chain, for example, when purchasing, storing, repackaging, relabeling; and during transportation and distribution. These guidelines were developed to assist in the various responsibilities involved at the different stages of the supply chain and to avoid associated risks such as the introduction of substandard and falsified medicinal products into the supply chain.

3.0 BACKGROUND / INTRODUCTION

3.1 Wholesale distribution forms part of the supply chain of manufactured medicinal products. Wholesalers are responsible for the effective, efficient and safe handling, storage and distribution of such products. These guidelines set out appropriate steps for meeting this responsibility.

3.2 Except for a brief mention under "storage", the guidelines do not deal with either common or statute law requirements such as the obligations of contractors, Occupational Health and Safety, Customs and Exercise, or the many legal requirements surrounding building construction. These must be understood by and met by the wholesaler.

3.3 Although this guideline refers to wholesaling, the scope includes medicine distributors and all premises that store medicinal products before distribution to other facilities.

4.0 DEFINITIONS

4.1 In these guidelines the word "**should**" indicates requirements that are expected to apply unless shown to be inapplicable or replaced by an alternative demonstrated to provide at least an equivalent level of quality assurance.

4.2 The word "**goods**" as used in this document refers to medicinal products.

4.3 **Good distribution practices (GDP)** - That part of quality assurance that ensures that the quality of a pharmaceutical product is maintained by means of adequate control of the numerous activities which occur during the distribution process, as

well as providing a tool to secure the distribution system from falsified, unapproved, illegally imported, stolen, substandard, adulterated and/or misbranded medicinal products.

4.4 Medicinal products:

4.4.1 Any substance or combination of substances presented as having properties for treating or preventing disease in human beings; or

4.4.2 Any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis.

4.4.3 However, a number of products are becoming difficult to classify as they fall within the scope of two definitions of a medicinal product on one hand and also of food supplements/food products, medical devices, biocides or cosmetics on the other hand. In such cases the stricter regime of medicinal products applies, with the ultimate aim being to protect the user.

5.0 GUIDELINES

5.1 BUILDINGS & GROUNDS

5.1.1 Warehousing of medicinal products should be carried out in buildings or parts of buildings that have been built for, or adapted to, this purpose.

5.1.2 The grounds should be established and maintained so as to minimize ingress into the buildings of dust, soil or other contaminants and should be maintained in an orderly condition. They should be free of accumulated waste, dirt and debris. Waste should be collected in designated closed containers and disposed of at frequent intervals.

5.1.3 Buildings should be kept free of rodents, vermin, birds, pets and pests.

5.1.4 Buildings should provide protection for the medicinal products from contamination and deterioration, including protection from excessive local heating or undue exposure to direct sunlight. The medicinal products received or dispatched at receiving or dispatch bays, platforms or areas should also be protected from dust, dirt and rain.

5.1.5 Buildings should have sufficient security to help prevent misappropriation of the medicinal products.

5.1.6 Sufficient space should be provided for the orderly receipt, warehousing and dispatch of medicinal products and, in particular, a quarantine area for isolation when necessary, including isolation of faulty packs and recalled goods. Each area in the wholesale should be physically separated and demarcated

5.1.7 Buildings and fixtures should be kept clean and well maintained. Cleaning equipment should be stored in hygienic conditions.

5.1.8 Sufficient lighting should be provided to enable all operations to be carried out accurately and safely.

5.2 FACILITIES

5.2.1 Storage facilities should protect goods from deterioration. The conditions of storage for the goods should be compatible with the storage conditions specified on their labels. All medicinal products should be stored off the floor.

5.2.2 Controlled storage environments, e.g. deep freeze, refrigeration, should be monitored, using suitable temperature recording devices and the records reviewed and filed. Refrigerated and freezing storage environments should be fitted with signals to indicate that refrigeration has failed. The signal should permit resetting only by an authorized person.

5.2.3 Temperatures in other areas where goods requiring specific storage conditions are held should be monitored and the results tabulated and analyzed so as to demonstrate the suitability of these areas for their purposes.

5.2.4 If any temperature is found to have deviated outside the relevant recommended conditions for an extended time, the manufacturer of the goods should be consulted and the suitability of the product for use resolved.

5.2.5 Special storage facilities should be provided for drugs of addiction, "Dangerous Drugs" , that is, a fixed lockable cupboard as detailed in the Dangerous Drugs Regulations (RGN 1111 of 1975)

5.2.6 Incompatible activities such as manufacture (including repackaging) or the handling of toxic chemicals should be avoided in areas in which medicinal products are handled by wholesale.

5.2.7 A written programme should be available indicating the frequency of cleaning and the methods to be used to clean the premises and storage areas.

5.3 EQUIPMENT

5.3.1 Instruments or equipment used for monitoring temperature (e.g. thermometers and integrated environmental management systems) should be calibrated on a regular basis to ensure their accuracy. Records for the calibration should also be kept on the premises.

5.3.2 Where electronic commerce (e-commerce) is used, i.e. electronic means for any of the steps, defined procedures and adequate systems should be in place to ensure traceability and confidence in the supply chain and products.

5.4 PERSONNEL

5.4.1 Pharmacists or Pharmacy Technicians bearing the responsibility for ensuring that products/materials are correctly handled, stored and distributed, should have the education, training experience or combination of these elements that will allow them to effectively discharge this responsibility.

5.4.2 Operating personnel should be trained to perform assigned duties and functions at an acceptable level. Records of any training relevant to their functions should be kept.

5.4.3 Procedures and job descriptions for employees and other persons having access to the products must be designed and administered to minimize the possibility of drugs coming into unauthorized possession.

5.4.4 During operating hours, the business must at all times be conducted under the continuous personal supervision of a licensed pharmacist or licensed pharmacy technician.

5.4.5 Premises dealing in dangerous drugs should be under the supervision of a licensed pharmacist.

5.5 STOCK HANDLING AND STOCK CONTROL

5.5.1 Handling and storage of medicinal products should be in accordance with established procedures designed to prevent contamination or deterioration, damage to packs or confusion of products. Particular care should be given to maintaining the integrity of seals on packs of sterile medicinal products. Attention should be paid to any special instructions from the manufacturer relating to handling or storage of the medicinal products.

5.5.2 Importers should take all reasonable measures to ensure that medicinal products are not mishandled or exposed to adverse storage conditions at ports of entry e.g. airports.

5.5.3 Storage, supply, distribution and recording of drugs of addiction, such as narcotics and psychotropic medicines, must be kept in accordance with applicable legislation.

5.5.4 Storage areas should be adequate and organized to permit segregation and identification of the various materials and products stored and should enable stored goods to be easily maintained in a clean, dry and orderly condition. Particular care should be taken to avoid mould growth in refrigerated rooms or cabinets.

5.5.5 There should be a system to ensure stock rotation, with frequent regular checks that the system is operating correctly. The system should ensure that pharmaceutical products due to expire first are sold and/or distributed first (FEFO). Where no expiry dates exist for the products, the FIFO principle should be applied. Products

beyond their expiry date or shelf-life should be removed from usable stock and neither sold nor supplied.

5.5.6 Spilled substances should be cleaned up promptly and rendered safe as quickly as practicable and under the supervision of a responsible person. A written procedure for dealing with spillage of items of special hazard, such as cytotoxic drugs, should be available.

5.5.7 Measures should be taken to demonstrate that restricted goods are not misappropriated.

5.5.8 Goods bearing an expiry date must not be received or supplied after their expiry date or so close to their expiry date that this date is likely to occur before the goods are used by the consumer. Such goods must be withdrawn from sale and quarantined pending disposal in accordance with agreements between the wholesaler and the supplier.

5.5.9 Precautions must be taken to prevent unauthorized persons from entering storage areas. Areas with medicines should be kept locked in the absence of the supervisor to restrict access by unauthorized persons.

5.6 INWARDS GOODS - FROM SUPPLIERS

5.6.1 Stock should be received and examined for correctness against order, for expiry date and for absence of damage.

5.6.2 There should be a system for the recognition and prompt handling of drugs of addiction, of those products requiring specific temperature storage, of products that have a short shelf life and of any other products that require special care.

5.6.3 Goods from suppliers rejected by the wholesaler because of error, breakage, leaking containers or other faults should be placed in quarantine until the matter is resolved with the supplier

5.7 DAMAGED GOODS FROM STOCK

5.7.1 Stock which has been damaged or withheld from sale and which is not immediately destroyed should be placed in quarantine until disposal so that it cannot be sold in error or, in the case of liquid leakage, cause contamination of other goods.

5.7.2 Stocks of products with broken seals, damaged packaging or suspected of possible contamination must not be sold or supplied.

5.8 RETURNED GOODS FROM CUSTOMER

5.8.1 All returned goods should be kept in quarantine. Goods which have left the care of the wholesaler should only be returned to saleable stock if:

5.8.1.1 They are in their original unopened containers, in good condition and bear valid expiry date;

5.8.1.2 It is not evident that they have been subject to adverse conditions;

5.8.1.3 They are packed separately from other goods and accompanied by a separate returns note; and

5.8.1.4 They have been examined and assessed by a person authorized to do so. Such assessment should take into account the nature of goods, and any special storage conditions they may require. If necessary, advice should be sought from the person responsible for the quality assurance of the manufactured product.

5.8.2 Reconditioning or repackaging (including relabeling) of medicinal products must not be carried out by wholesalers unless such activity is specifically exempted from the requirement to hold a manufacturers license.

5.9 RETURNED GOODS - FROM RECALL

5.9.1 There should be a written procedure detailing the action to be taken in recalling goods on behalf of their manufacturer or sponsor, subject to any amendment necessary in specific circumstances. This procedure should be consistent with the "Recall Procedure for Pharmaceutical Goods" issued by the Authority. The wholesaler should be able to facilitate a recall procedure relative to the area to which goods have been supplied. Recalls carried out should be documented and records of all recalled goods received into the warehouse should be kept. A person should be designated as responsible for execution and co-ordination of recalls.

5.10 REJECTED GOODS

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

5.11 DISPATCHED GOODS - TO CUSTOMERS

5.11.1 There should be a written procedure detailing the action to be taken in dispatching goods to customers.

5.11.2 This procedure should ensure that orders are collected by recognized and approved persons only, regardless of the means of settlement of the account (cash or credit). The procedure should also have provisions for the recording of collector's national identification details.

5.11.3 Wholesale dealers shall encourage their customers to have representatives authorized to collect orders on behalf of the approved person/premises. The wholesaler shall maintain a list of the approved representatives in the dispatch area as an attachment to the Standard Operating Procedure on dispatching orders

5.12 Records for the dispatch of pharmaceutical products should be prepared and should include at least the following information:

5.12.1 Date of dispatch;

5.12.2. Name and address of the entity responsible for the transportation;

5.12.3 Name, address and status of the addressee (e.g. retail pharmacy, hospital, community clinic);

5.12.4 a description of the products including, e.g. name, dosage form and strength; and quantity of the products, i.e. number of containers and quantity per container;

5.12.5 assigned batch number and expiry date;

5.12.6 applicable transport and storage conditions; and

5.12.7 a unique number to allow identification of the delivery order.

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

5.14 TRANSPORT

5.14.1 Containers for delivery of goods should be clean and provide adequate protection for the goods delivered.

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

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

5.14.4 Goods labelled to require refrigerated storage should, where appropriate, be transported in insulating containers with ice or other cooling agent. The agent should not cause freezing of goods marked 'Refrigerate - do not freeze'. Goods labeled to require frozen storage should be transported in such a way that they remain frozen. Where appropriate, the transport packaging should be fitted with devices to detect exposure to conditions outside specific limits.

5.14.5 Delivery of other goods requiring controlled temperatures should be carried out by the fastest practical means. These goods may, in suitable circumstances, remain temporarily outside the specified temperature range while delivery is in progress. However, in assessing suitable conditions for delivery in any particular case, due account should be taken of the time required for delivery, prevailing or likely weather conditions and the nature of goods and their labeled storage requirements. Special procedures should be established for goods likely to be exposed to unfavourable environments over holiday periods.

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

5.15 COMPLAINTS

5.15.1 Complaints regarding the product or its packaging, as distinct from those relating solely to matters within the wholesalers control, must be notified promptly to the manufacturer or sponsor of the goods. Complaints relating to the wholesalers' own activity should be evaluated and measures taken, where appropriate, to prevent their recurrence.

5.16 DOCUMENTATION AND RECORDS

5.16.1 Written procedures should describe the different operations which may affect the quality of the products or of the distribution activity: receipt and checking of deliveries, storage, cleaning and maintenance of the premises, (including pest control), recording storage conditions, security of stocks and on site, consignments in transit, withdrawal from saleable stock records, including records of clients orders, returned products, recall plans, etc. These procedures should be approved, signed and dated by the person responsible for the quality system.

5.16.2 Invoices or packaging slips should be issued for each delivery and accompany the goods.

5.16.3 Clear and readily available records should be maintained showing the receipt and disposal of all products purchased and sold. Such records should be kept in an accessible form and place for the appropriate legislated period. (Currently five years)

5.16.4 An updated list of all premises allowed to store, dispense or sell drugs should be available at all premises to ensure medicines are only sold to these persons or premises.

5.16.5 Keep records of each sale or purchase, showing date of purchase (supply), name of medicinal product, quality received (or supplied) name and address of suppliers or consignee. Records should ensure traceability of the origin and destination of products, e.g. by use of batch numbers in-order that they can be identified. This information is detailed in the legislation.

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

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

5.17 SUBSTANDARD AND/OR FALSIFIED MEDICINAL PRODUCTS

5.17.1 Should be kept in a designated area apart from other medicinal products to avoid confusion. Clearly labeled as "NOT FOR SALE". The MCAZ and the holder of the products' registration should immediately be informed.

5.18 SALE OF UNREGISTERED MEDICINAL PRODUCTS

5.18.1 This is not allowed, but should written permission under the appropriate provisions be given by the MCAZ e.g. Section 75 of the Medicines and Allied Substances Act *(Chapter 15:03)* the following should be observed:

5.18.1.1 Records of sales should be kept as in Section 5.16 above. This may also include special conditions imposed by the MCAZ on giving the permission; and

5.18.1.2 The medicines should be stored separately from other registered medicines. The area should be clearly indicated as to its use to ensure adequate controls of sales.

5.18.1.3 The current registers of approved medicines and approved persons should be available to avoid selling unregistered medicines and/or to unlicensed premises.

5.19 MINIMUM DIMENSIONS OF PREMISES

5.19.1 The minimum area of the different areas of the wholesale should be as follows:

5.19.1.1 Receiving area: 10 square metres

5.19.1.2 Quarantine area: 5 square metres

5.19.1.3 Warehouse area: 15 square metres

5.19.1.4 Dispatch area: 10 square metres

5.20 IMPORTATION

5.20.1 All reasonable steps should be taken by importers to ensure that products are not mishandled or exposed to adverse storage conditions at ports of entry or airports.

5.20.2 Import documentation for all consignments should be kept at the premises for the legislated period of time. (Currently five years)

6.0 KEY RELEVANT DOCUMENTS

6.1 Medicines and Allied Substances Control Act (Chapter 15:03)

6.2 Medicines and Allied Substances Control (General Regulations), SI 150 of 1991

6.3 Good Storage and Distribution Practices for Medical Products (WHO)

6.4 Medicinal Products in the European Union, The legal framework for medicines for human use (2015)

7.0 HISTORY

DOCUMENT HISTORY		
Revision Number	Date Approved	Reason for Change and Amendments
4	October 2014	**Date Reviewed:** February 2020 **Reason for change and amendments** Rolling Review and Continuous Improvement aligning the guideline to the requirements of the new template The following changes were done from **Revision 4** to **Revision 5** **Description of Changes** **Added** **4.0 DEFINITIONS** **4.3 Good distribution practices (GDP)** - That part of quality assurance that ensures that the quality of a pharmaceutical product is maintained by means of adequate control of the numerous activities which occur during the distribution process, as well as providing a tool to secure the distribution system from falsified, unapproved, illegally imported, stolen, substandard, adulterated and/or misbranded medicinal products. **4.4 Medicinal products:** 4.4.1 Any substance or combination of substances presented as having properties for treating or preventing disease in human beings; or 4.4.2 Any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis. 4.4.3 However, a number of products are becoming difficult to classify as they fall within the scope of two definitions of a medicinal product on one hand and also of food supplements/food products, medical devices, biocides or cosmetics on the other hand. In such cases the stricter regime of medicinal products applies, with the ultimate aim being to protect the user. **3.6 changed from**

		Sufficient space should be provided for the orderly receipt, warehousing and dispatch of pharmaceuticals and, in particular, a quarantine area for isolation when necessary, including isolation of faulty packs and recalled goods. Each area in the wholesale should be physically separated and demarcated **To** **5.1.2** Sufficient space should be provided for the orderly receipt, warehousing and dispatch of medicinal products and, in particular, a quarantine area for isolation when necessary, including isolation of faulty packs and recalled goods. Each area in the wholesale should be physically separated and demarcated **Added** **5.2 FACILITIES** **5.2.3 (New)** Special storage facilities should be provided for drugs of addiction, "Dangerous Drugs" , that is, a fixed lockable cupboard as detailed in the Dangerous Drugs Regulations (RGN 1111 of 1975) **5.2.4 (New)** Incompatible activities such as manufacture (including repackaging) or the handling of toxic chemicals should be avoided in areas in which medicinal products are handled by wholesale. **5.2.5 (New)** A written programme should be available indicating the frequency of cleaning and the methods to be used to clean the premises. **6.1.1 changed from** Handling and storage of pharmaceuticals should be in accordance with established procedures designed to prevent contamination or deterioration, damage to packs or confusion of products. Particular care should be given to maintaining the integrity of seals on packs of sterile pharmaceuticals. Attention should be paid to any special instructions from the manufacturer relating to handling or storage of the pharmaceuticals. **To** **5.5.1** Handling and storage of medicinal products should be in accordance with established procedures designed to prevent contamination or deterioration, damage to packs or confusion of products. Particular care should be given to maintaining the integrity of seals on packs of sterile medicinal products. Attention should be paid to any special instructions from the manufacturer relating to handling or storage of the medicinal products. **6.1.2 changed from** Importers should take all reasonable measures to ensure that pharmaceuticals are not mishandled or exposed to adverse storage conditions at ports of entry e.g. airports. **To**

		5.5.2 Importers should take all reasonable measures to ensure that medicinal products are not mishandled or exposed to adverse storage conditions at ports of entry e.g. airports. **6.5.2 changed from** Reconditioning or repackaging (including relabeling) of pharmaceuticals goods must not be carried out by wholesalers unless such activity is specifically exempted from the requirement to hold a manufacturers license. **To** **5.8.2** Reconditioning or repackaging (including relabeling) of medicinal products must not be carried out by wholesalers unless such activity is specifically exempted from the requirement to hold a manufacturers license. **10.0 changed from** **COUNTERFEIT MEDICINAL PRODUCTS** **To** **5.17 SUBSTANDARD AND/OR FALSIFIED MEDICINAL PRODUCTS** **<u>12.0 changed from</u>** **12.0 MINIMUM DIMENSIONS OF PREMISES** **12.1** The minimum area of the different areas of the wholesale should be as follows: Receiving area: 10 square metres Quarantine area: 5 square metres Warehouse area: 15 square metres Dispatch area: **To** **5.19 MINIMUM DIMENSIONS OF PREMISES** 5.19.1 The minimum area of the different areas of the wholesale should be as follows: 5.19.1.1 Receiving area: 10 square metres 5.19.1.2 Quarantine area: 5 square metres 5.19.1.3 Warehouse area: 15 square metres 5.19.1.4 Dispatch area: 10 square metres **Added 6.0(New)** **6.0 KEY RELEVANT DOCUMENTS** **6.1 Medicines and Allied Substances Control Act (Chapter 15:03)** **6.2 Medicines and Allied Substances Control (General Regulations), SI 150 of 1991**

		6.3 Good Storage and Distribution Practices for Medical Products (WHO) **6.4 Medicinal Products in the European Union, The legal framework for medicines for human use (2015)**