RWANDA FDA
Rwanda Food and Drugs Authority

GUIDELINES ON COLD CHAIN MANAGEMENT FOR VACCINES & OTHER BIOPHARMACEUTICAL PRODUCTS

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GUIDELINES DEVELOPMENT HISTORY

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FOREWORD

Rwanda Food and Drugs Authority is a regulatory body established by the Law N° 003/2018 of 09/02/2018. One of the functions of Rwanda FDA is to regulate matters related to quality, safety and efficacy of distributed medical products in Rwanda.

Considering the provisions of the regulations N° CBD/TRG/001 Rev. N° 1, governing authorization to manufacture, to operate as wholesale and retail seller of medical products. The authority Issues Guidelines N° DIS/GDL/056 *Guidelines on cold chain management for vaccines & other biopharmaceutical Products.*

These guidelines provide guidance to the distributors of medical products particularly on good cold chain management for vaccines & other biopharmaceutical products guideline. Distributors of medical products are encouraged to familiarize with this guideline and follow them when distributing medical products.

Adherence to these guidelines will ensure that relevant information is provided for distribution of medical products. This will facilitate efficient and effective distribution of medical products with assured quality, safety and efficacy. It will also help to avoid malpractices in the distribution process of medical products.

The Authority acknowledges all the efforts of key stakeholders who participated in development and validation of these guidelines.

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13/09/2021

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Director General

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ABBREVIATIONS AND ACRONYMS

GDP	Good Distribution Practices
GMP	Good Manufacturing Practices
GSP	Good Storage Practices
SOP	Standard Operating Procedures
LTR	Local Technical Representative

CHAPTER 1. INTRODUCTION

1.1 PURPOSE OF THESE GUIDELINES

The purpose of this document is to provide guidance to importers and owners of storage facility for medicines that require cold chain management. This is to provide stakeholders the relevant regulatory requirements needed to maintain the compliance status of their operational activities and to ensure that the quality and efficacy of the product will not be compromised.

The document provides useful regulatory insight into the receipt, storage, release, distribution and cold chain management of vaccines and other biological products. Applicants are encouraged to familiarize themselves with the information contained in this document prior to applying for a license import or distribute a cold chain product.

Health facilities are required to maintain the cold chain to ensure that temperature sensitive medicines reach consumers in good quality. Cold chain management is a specialized area of biopharmaceutical products management which begins when a biopharmaceutical product is manufactured, stored and moves through the distribution chain till it gets to the end user at the time of administration. It is required that the product be held and distributed in a controlled environment. The products lose their potency if they are exposed to temperatures outside the required range of +2˚C to +8˚C or other cool storage as recommended by manufacturers or when exposed to light .

Loss of potency of medicines may lead to increased disease burden, medical costs to patients and wastage of supplies. In addition, the loss of effectiveness of vaccine and other biologics is cumulative and cannot be reversed. Therefore, it is considered critical to have adequate control of all steps and procedures involved both in manufacturing and quality control, storage and distribution, to ensure that product quality is maintained.

Last but not least, personnel along the supply chain must implement proper handling of temperature-sensitive products, and all equipments used for recording, monitoring and maintaining temperature and humidity conditions should initially be validated and thereafter calibrated on a regular basis.

Anyone handling biopharmaceutical products is responsible for their potency, at each step in the transport and storage since these products are delicate biological substances that can become less effective or destroyed if they are:

1. Frozen
2.Exposed to heat
3. Exposed to direct sunlight or fluorescent light
4 .The loss of effectiveness of vaccine and other biologics is cumulative and cannot be reversed

1.2 SCOPE

These guidelines apply to any person, institution, business company engaging in the manufacturing and sale of medical products.

These guidelines are for the interest of individuals intending to engage in importation and distribution of vaccines and other biopharmaceutical products in Rwanda.
This prescribes the minimum Good Storage Practices (GSP) and Good Distribution Practices (GDP) requirements for the facilities for storage and distribution of vaccines and other biopharmaceutical products to ensure quality and safety.

It is necessary to emphasize that, no regulated product should be manufactured, imported, exported, advertised, sold or distributed in Rwand unless it has been registered in accordance with the legal provisions of the Food, Drugs and Related Products and the accompanying guidelines.

Vaccines and other biopharmaceutical products should not be imported into Rwanda unless the facility has been inspected and found to comply with Good Storage Practice and Good Distribution Practice.

CHAPTER II: INTERPRETATION

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.

"**Authority**" means the Rwanda Food and Drugs Authority or its acronym "Rwanda FDA", established under the article 2 of the Law No. 003/2018 of 09/02/2018.

"Biopharmaceutical (biological or biologic) products" means substances or materials that are derived from living organisms (e.g. bacteria, fungi, vaccines, animals, humans etc) and are extracted and/or purified for use as a preventative, therapeutic or diagnostic tool

The"**cold chain**" is a system of storing and transporting temperature-sensitive products at recommended temperatures from the point of manufacture to the point of use .

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

"Contamination" means the undesired introduction of impurities of a chemical or microbiological nature, or of foreign matter, into or on to a starting material, intermediate or medical product during handling, production, sampling, packaging or repackaging, storage, distribution or transportation.

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

"Counterfeit medical product"A medical product that is deliberately and fraudulently mislabelled with respect to identity and/or source. Counterfeiting can apply to both branded and generic products, and counterfeit medical products may include products with the correct ingredients, with the wrong ingredients, without active ingredients, with an incorrect quantity of active ingredient or with fake packaging.

"Distribution"The procuring, purchasing, holding, storing, selling, supplying, importing, exporting, or movement of medical products, with the exception of the dispensing or providing medical products directly to a client.

"Distributor" means a intermediary entity between the producer of a medical product and another entity in the distribution channel or supply chain.

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

"Forwarding agent" means 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)" is that part of quality assurance that ensures that the quality of a medical 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 counterfeits, unapproved, illegally imported, stolen, counterfeit, substandard, adulterated, and/or misbranded medical products.

"Good Manufacturing Practices (GMP)" is that part of quality assurance that ensures that medical products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization.

"Good Pharmacy Practice (GPP)" is the practice of pharmacy aimed at providing and promoting the best use of medicines and other health care services and products, by patients and members of the public. It requires that the welfare of the patient is the pharmacist's prime concern at all times.

"Good Storage Practices (GSP)" is that part of quality assurance that ensures that the quality of medical products is maintained by means of adequate control throughout the storage thereof.

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

"Importer" means an individual or entity that undertakes the act of importation

"Labelling" means Process of identifying a medical product including the following information, as appropriate: name of the product; active ingredient(s), type and amount; batch number; expiry date; special storage conditions or handling precautions; directions

for use, warnings and precautions; names and addresses of the manufacturer and/or the supplier.

"Manufacture" means all operations of purchase of materials and products, production, packaging, labelling, quality control, release, storage and distribution of medical products, and the related controls.

"Pharmaceutical product" means any substance capable of preventing, treating human or animal diseases and any other substance intended for administration to a human being or an animal in order to diagnose diseases, restore, correct or carry out modification of organic or mental functions. It also means products used in disinfecting premises which food and drugs are manufactured, prepared or stored, cleaning hospitals, equipment and farm houses.

"Product recall" means a process for withdrawing or removing a medical product from the supply chain because of defects in the product, complaints of serious adverse reactions to the product, unauthorised entry on to the market and/or concerns that the product is or may be counterfeit. The recall might be initiated by the manufacturer, importer, Local Technical Representative (LTR) wholesaler, distributor or The Authority.

"Medical product" Includes medicines, vaccines, diagnostics and medical devices

"Quality assurance" is 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 medical products are of the quality required for their intended use.

"Quality system" is 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" means the status of medical products isolated physically or by other effective means while a decision is awaited on their release, rejection or reprocessing.

"Retailer" is an entity authorised to carry on the business of dispensing or providing medical products directly to a patient or his or her agent only. Retailers are not authorised to supply medical products to distributors or other retailers.

"**Sampling**" means operations designed to obtain a representative portion of a medical product, based on an appropriate statistical procedure, for a defined purpose, e.g. acceptance of consignments or batch release.

"**Shelf-life**" means the period of time during which a medical product, if stored correctly, is expected to comply with the specification as determined by stability studies on a number of batches of the product. The shelf life is used to establish the expiry date of each batch.

"Standard Operating Procedure (SOP)" is an authorized, written procedure giving instructions for performing operations not necessarily specific to a given product but of a more general nature (e.g. equipment operation, maintenance and cleaning, validation, cleaning of premises and environmental control, sampling and inspection).

"Storage" means the storing of medical products up to the point of use.

"Supplier" is a person or entity engaged in the activity of providing products and/or services.

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

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

"Wholesale Pharmacy (wholesaler)" is an entity that is authorised to carry on the business of selling medical products in large quantities to other authorised sellers with the exception of dispensing or providing medical products directly to a patient.

CHAPTER III: REQUIREMENTS FOR A COLD CHAIN STORAGE FACILITY

3.1. GENERAL CONSIDERATIONS

3.1.1 Location and Surroundings: The cold storage facility should be located at a place which should be away from open sewage, drain, public lavatory or similar unhygienic surroundings.

3.1.2 Building/facility: The building(s), used for the storage and maintenance of cold chain of vaccine and other biopharmaceutical products should be constructed in such a manner as to permit the operation of its activity under hygienic conditions and should avoid the entry of insects, rodents and flies. The facility should be well lighted, ventilated and screened (mesh), wherever necessary. The facility should have an area of reasonable size for its operations. The walls and floors of the rooms, where storage equipment are kept should be smooth, washable and capable of being kept clean.

3.1.3 General health and sanitation, and protective clothing: The employees should be free from contagious or infectious diseases. They should be provided with clean adequate protective apparel. There should be adequate, clean and convenient hand washing and toilet facilities.

3.2 PERSONNEL

3.2.1 There should be sufficient number of personnel to suit operations of the facility.

3.2.2 Persons in charge of cold chain facility should have a minimum of Ordinary National Diploma (OND) in a relevant science discipline.

3.2.3 The Superintendent Pharmacist of the organization should have a current annual license to practice.

3.2.4 Personnel should wear protective apparel.

3.2.5 Personnel should practice good sanitation and hygiene practices.

3.2.6 Personnel should undergo medical fitness test at least once a year and the records should be kept.

3.2.7The cold chain is a family that requires regular, consistent supervision. Failing to do so, lead to almost daily cold chain rupture (which goes unnoticed due to lack of monitoring).

3.3. EQUIPMENT

3.3.1 Equipment used in the storage, release and distribution of vaccines and other biopharmaceutical products should be maintained, located and operated in accordance to the manufacturers' instructions.

3.3.2 The equipment should be regularly observed and calibrated in accordance with an approved SOP and should operate in the manner for which it was designed.

3.3.3 Equipment should be calibrated relatively frequently in order to establish accuracy, i.e. their meteorological stability or the change in their measuring ability between calibrations.

3.3.4 REFRIGERATOR/CHILLERS

3.3.4.1 Combination refrigerator/freezer units sold for home use are not adequate for vaccines and other biopharmaceutical products storage as domestic refrigerators do not have good temperature control.

3.3.4.2 However, if the refrigerator and freezer compartments each have a separate door, vaccines and other biopharmaceutical products should not be stored near the cold air outlet from the freezer to the refrigerator. It should be ensured that the door to the refrigerator closes properly, the rubber seals are not broken and the hinges adjusted if necessary.

3.3.4.3 The refrigerator should be placed in an air-conditioned room, away from direct heat or sunlight, at least 20cm to 30cm from the wall and with at least 40cm of clear space above. The room should be well ventilated so that the heat from the refrigerators and chillers will not heat up the room. If several refrigerators or freezers are kept in one room, they should be properly spaced, at least 30cm from each other.

3.3.4.4 The refrigerator/chillers should be properly labelled and identified.

3.3.4.5 At least 50% of the space in the refrigerator should be filled at all times to allow for adequate circulation of cold air, and to stabilize the refrigerator temperature.

3.3.4.6 The products should be maintained at the manufacturer's recommended temperature range. NOTE: Food and drink should not be stored in a refrigerator used for vaccine/biopharmaceutical storage. Frequent opening of the refrigerator to retrieve food items can affect the temperature of the unit and thus affect the efficacy of the products.

3.3.5 FREEZERS

4.3.5.1 Freezers used to condition ice packs used in the transportation of vaccines and other pharmaceutical products should be maintained in like manner as the refrigerator and chillers.

3.3.6 WALK-IN REFRIGERATION UNITS

3.3.6.1 A calibrated max/min thermometer should be placed inside the unit for use as a back-up and to confirm the temperature indicated on the recorder.

3.3.6.2 Products should not be stored next to the door and goods sensitive to temperatures below 2°C should not be placed in the airflow from the refrigeration unit.

3.3.6.3 Probes should be sited within an appropriate load simulator so that transient rises in temperature (such as might occur when a door is opened) do not trigger the alarm. The probes should be sensitive and efficient to detect temperature excursions.

3.3.6.4 The walk-in chamber should have in-built alarm systems. The low temperature alarm must trigger before the temperature drops below +2°C and before excursion to 8°C. The temperatures must be checked twice each day, 7 days a week, all year round.
3.3.6.5 Temperature mapping should be repeated if significant changes take place, such as the repair or replacement of the refrigeration unit or changes to the internal storage layout.

3.3.6.6 There should be access control in place.

3.3.7 WATER PACKS

3.3.7.1 Water packs are leak-proof plastic containers that can be filled with tap water. They are used to line the inside of the cold box.

3.3.7.2 Water packs are used to keep vaccines at the required temperature range inside cold boxes and carriers.

3.3.7.3 It is important to use the correct number and size of water packs and to follow the instructions printed inside the lid of the container.

3.3.7.4 The appropriate temperature of the water pack will depend on the type(s) of products being transported, the ambient temperatures to which the cold box or carrier will be exposed, and the duration of transport.

3.3.8 COLD BOXES

3.3.8.1 These are insulated containers that can be lined with water packs to keep vaccines, diluents and other biologics in the required temperature range during transport or short-term storage.

3.3.8.2 The duration for which the cold boxes can maintain the recommended storage temperature should be validated.

3.3.8.3 Once packed, cold boxes should not be opened until the products are needed.

3.3.8.4 The cold box to be used should be chosen based on the storage capacity needed for the supply period, temperature required and number of water packs compatible with the size of the cold box.

Note: It is important to use the correct number and size of water packs.

3.3.8.5 The following steps should be followed when packing a cold box:

3.3.8.5.1 Remove fully frozen ice-packs from the freezer and leave to thaw for a few minutes to allow the surface frost melt. If there is frost, the temperature may be between -15°C and -25°C and susceptible products may be damaged if they come into direct contact with it.

3.3.8.5.2 Line the bottom and sides of the cold box with fully frozen ice packs.

3.3.8.5.3 Place the products and pre-cooled diluents into the cold box. Do not place products in direct contact with ice packs.

3.3.8.5.4 Cover the products and its diluents with the frozen icepacks (but ensuring that they do not come in direct contact with the products) and replace the lid. Secure the lid tightly. Keep the cold box in the shade.

3.3.9 TEMPERATURE MONITORING DEVICES

3.3.9.1 These are the instruments used to monitor and record the storage temperature of the products such as stem thermometers, in-built thermometers and temperature loggers.

3.3.9.2 The instruments should be calibrated within the required range of storage.

3.3.9.3 Calibration should be documented and evidence of calibration should be readily available and should show the reference standards used.

3.3.10 PREVENTIVE MAINTENANCE

3.3.10.1 A preventive maintenance schedule be developed and implemented for all equipment and the frequency should be increased as the equipment age increases.

3.3.10.2 Preventive maintenance activities should include but not limited to the following:

3.3.10.2.1 Equipment breakdowns should be reported immediately.

3.3.10.2.2 Regular checks of refrigerator seals to ensure cold air does not leak. If seals are brittle or torn they should be replaced.

3.3.10.2.3 Area around the refrigerator should be kept clean and dust free.

3.3.10.2.4 The contingency plan should be availed. This is the list of actions to be taken in case of a power failure, or of equipment malfunction. It must answer the following questions: Thinking about, and finding answers to, these questions before the problem arises means you will not lose time when the situation actually happens.

CHAPTER IV: COLD CHAIN MAINTENANCE

4.1 QUALITY MANAGEMENT SYSTEM

4.1.1 The Quality Management System (QMS) is a management tool set out to ensure that measures are in place to ensure compliance in all areas of the Cold Chain maintenance, from receiving, storing and dispatching of the vaccines and other biopharmaceutical products.

4.1.2 The basic elements of quality management are: An appropriate infrastructure or "quality system", encompassing the organizational structure, procedures, processes and resources. Also, a systematic action necessary to ensure adequate confidence that a product (or service) will satisfy given requirements for quality.

4.1.3 The QMS appropriate to the handling of these pharmaceutical products should ensure that:

4.1.3.1 All procedures are clearly specified in a written form and adequately implemented.

4.1.3.2 Personnel responsibilities are clearly specified in job descriptions.

4.1.3.3 Processes are in place to assure the management of outsourced activities.

4.1.3.4 Satisfactory arrangements exist to ensure that the pharmaceutical products are stored, distributed and subsequently handled such that quality is maintained throughout the storage and transportation period.

4.1.3.5 The organization should have an organizational chart. Personnel inresponsible positions should have adequate authority to carry out their responsibilities. Their duties may be delegated to designated deputies of satisfactory qualification.

4.1.3.6 The organization should have adequate number of personnel with the necessary qualifications and practical experience.

4.1.3.7 All personnel should receive initial and continuing training, including hygiene instructions.

4.1.4 DOCUMENTATION - Standard Operating Procedures (SOPs) should be in place to describe all operations which are likely to affect the quality of products . These include the reception of deliveries, storage conditions and transportation of the medicines. All these are necessary in maintaining the quality of medicines and protecting patients from consuming sub-standard or ineffective medicines.

4.1.5 RECORDS- The records which the organization is required to maintain should include but not limited to the following:

4.1.5.1 Receipt of vaccine/ other biologic records: It should indicate details of products received and condition of receipt.

4.1.5.2 Daily temperature monitoring chart: It should indicate the temperature reading taken at least twice daily and signed by the authorized person.

4.1.5.3 Distribution record: It should indicate the details of the product distributed and the temperature at point of delivery.

4.2 STORAGE OF VACCINES AND OTHER BIOPHARMACEUTICALS

5.2.1.1 The products should be stored at temperatures between the ranges of 2°C to 8°C unless otherwise specified by the manufacturer. For instance,vaccines produced with viral and/or lyophilized strains can be stored at temperatures between -15°C and -25°C.

4.2.1.2 The shelf-life assigned to the products by the manufacturer should be adhered to.

4.3 DISTRIBUTION SYSTEM

4.3.1.1 Records of product distribution network must be properly kept for easy recall of defective products.

4.3.1.2 Distributors names, addresses, telephone numbers, email addresses, quantity of products issued, batch numbers, dates of manufacture and expiry should be maintained.
4.3.1.3 Record of maintenance of cold chain along distribution channel should be maintained.

4.4 TRANSPORTATION AND HANDLING

4.4.1 Products should be handled and transported under conditions specified by the manufacturer to maintain the cold chain to prevent deterioration, spoilage and breakage to ensure that the product quality is maintained up to the time of delivery to the consumer.

4.4.2 Arranging vaccines/other biopharmaceutical products inside cold chain equipment - Products must be arranged inside cold chain equipment in a manner that helps ensure that they remain in good condition with minimum risk of exposure to damaging temperatures. This section describes how to arrange the products inside refrigerators, cold boxes and carriers. The products should be arranged such that:

4.4.2.1 Vaccines its diluents and other biopharmaceuticals should be in a refrigerator that is reserved for this purpose only. If other heatsensitive supplies, such as drugs, ointments, sera and samples, have to be stored in the refrigerator, label them clearly and keep them completely separate from the vaccines its diluents and other biologics.

4.4.3 Air can circulate freely; this also makes it easier to handle the products.

4.4.4 Products supplied in their original cartons, the boxes should be at least two-centimeter space between stacks. The cartons should be marked clearly and the markings are visible when the door or lid is opened.

4.4.5 Products are supplied as individual containers (vials, ampoules or tubes), use a plastic tray, plastic box or other arrangement to store in an orderly fashion and labeled sections for easy identification.

4.4.6 If diluent is packaged with their products, store the complete packaged product in the refrigerator. If diluents are supplied separately from the products, they should also be stored in the refrigerator.

NOTE:

- Never store food or drink in refrigerator used for storage of vaccine/biopharmaceutical products. Do not open the door or lid unless it is essential to do so. Frequent opening raises the temperature inside the refrigerator.
- If there is a freezer compartment, do not use it to store biologics and diluents except stipulated by manufacturer.
- Do not keep expired biologics in the refrigerator/chiller /walk-in units.

- Do not keep vaccines with VVMs that have reacted, or are beyond, their discard point. Discard all these items immediately according to Rwanda FDA requirement for destruction.

4.5 COMMUNICATION

- It is in Rwanda FDA obligation to communicate strategy to ensure all stakeholders and implementing parties are well informed about the relevant policies, guidelines and SOPs for the cold chain management
- Officer responsible for managing the cold chain and supply chain systems should have written and clearly defined roles and responsibilities .
- Establish a coordination mechanism to ensure timely notification and response to incidents related to none- compliance.

ENDORSEMENT OF THE GUIDELINES

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