LIBERIA MEDICINES & HEALTH PRODUCTS REGULATORY AUTHORITY (LMHRA)

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GUIDELINE FOR LABELING, PACKAGING AND DISTRIBUTION OF IN-VITRO DIAGNOSTICS

Version No 002

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The LMHRA will welcome comments for improvement of the guideline during implementation.

LIST OF ABBREVIATIONS

LMHRA	Liberia Medicines & Health Products Regulatory Authority
IVD(s)	In-Vitro Diagnostic(s)
WHO	World Health Organization
IDE	Investigational Device Exemption
MVTR	Moisture Vapor Transmission Rate

GLOSSARY

For the purpose of these guidelines the following terms shall be defined as follows:

Bulk product = Any product which has completed all processing stages up to, but not including packaging.

Label = any legend, word or mark attached to, included in, belonging to or accompanying an IVD or package.

Lot or batch number = the number or a combination of numbers and letters specifically given to the IVD which is linked to the manufacturing history of the drug

Material Safety Data Sheet = A document that contains information on the potential health effects of exposure to chemicals or other potentially dangerous substances, and on safe working procedures when handling chemical products.

Organoleptic Evaluation = Use of sense organs to assess the quality of a product/IVD.

Package = any suitable container in which the IVD is wholly or partly placed or packed.

Primary Package = The layer of packaging in immediate contact with the product.

Secondary Package = The layer of packaging more visible to the consumer in retail displays.

Sequelae = A condition that is the consequence of a previous disease or injury.

Tamper-proof = A condition in which a packaging is done to prevent interference or change.

INTRODUCTION

The registration of In-Vitro Diagnostics (IVDs) in Liberia is governed by the provisions and requirements of the LMHRA Act of September, 2010. IVDs are those reagents, instruments, and systems intended for use in diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body.

The safe use of IVDs depends on users carefully reading the information on labeling and packaging and accurately and being able to assimilate and act on the information presented. The primary purpose of labeling and packaging is to reduce ambiguous identification of the IVD and the conditions for its safe use. Inappropriate packaging can lead to product mix-up, loss of product identity, contamination, cross-contamination and lack of stability data to support expiry dates.

Usually IVDs are distributed in their original package provided and labeled by the manufacturer. In some instances, the manufacturer supplies IVDs as bulk product and there may be a need to repackage for distribution. Other reasons may also necessitate the need for repackaging and/or labeling such as convenience for the practitioner, reduction of waste and conservation of supplies and reduction of costs (in a few cases).

Also, IVDs are handled at different levels of the supply chain before reaching the users. Therefore, this Guideline also addresses the various areas, activities and roles of the personnel involved in the handling of IVDs in the entire supply chain.

Hence, in the exercise of the power conferred on the LMHRA through the 2010 Act and all the powers enabling it in that behalf, the LMHRA herewith proposes the following Guideline for the Labeling, Packaging and Distribution of IVDs used in Liberia which should be adhered to.

Purpose and Scope

These regulations are intended to:

- Ensure that no person shall manufacture, import, export, distribute, advertise, display for sale or sell any IVD that is not adequately labeled;
- Guide the processes of re-packaging and re-labeling of IVDs as may be necessary;
- Control the activities of the supply chain management which includes storage, transportation and distribution of IVDs in both the public and private health sectors.

These regulations shall apply to all labeling and packaging of IVDs. They are also applicable to all manufacturers or importers of IVDs in the conduct of re-packaging and re-labeling, as well as the storage and distribution of IVDs.

CHAPTER 1

REQUIREMENTS FOR LABELING AND PACKAGING

1.1 General Requirements

The following basic information are required on the label of all IVDs:

1.1.1 The established and proprietary names of the product;

1.1.2 The intended use or uses, e.g., HIV-1 diagnosis, *Plasmodium falciparum* detection, etc.;

1.1.3 A statement of warnings or precautions for users and any other warnings appropriate to user hazards, and a statement "For In Vitro Diagnostic Use";

1.1.4 Name and place of manufacturer's business, packager, or distributor (**NOTE**: indicating the name and address of the manufacturer and packer is a must);

1.1.5 English labels with Times New Roman Font Size 12 to contain the required information for adequate legibility (***foreign language translation is optional but should be clearly differentiated from the primary English labels***);

1.1.6 Lot or batch number traceable to the production history;

1.1.7 The label may be used on both primary and secondary packages, or should be easily legible through the outermost package if it appears only on the primary package;

1.1.8 The information may appear on the outermost package, instead of the label if the presence of any label information will interfere with the test;

1.1.9 The primary package must be capable of bearing labels with sufficient space;

1.1.10 The information being affixed to the package has to be the permanent (indelible) type in a tamper-proof way so that any attempt to remove the label will create permanent damage to the packaging;

1.1.11 Stamping with ink is not allowed.

1.2 Specific Requirements

1.2.1 Multiple unit products must have traceability of the individual units;

1.2.2 A multiple unit product that requires use of its components as a system should have the same lot number, or other suitable uniform identification, on all units.

1.2.3 **Reagents**:

1.2.3.1 The container must bear the Established (common or usual) name;

1.2.3.2 Quantity, proportion, or concentration of all active ingredients must be included on the container; e.g., mg. weight per unit volume, mg./dl etc.,

1.2.3.3 Relevant information for reagents derived from biological materials must be provided;

1.2.3.4 Appropriate cautions or warnings on the use and handling of reagent must be given; the statement: "For In Vitro Diagnostic Use"; and any other limiting statements appropriate to the intended use of the product must be indicated;

1.2.3.5 A statement of purification or treatment required for use;

1.2.3.6 Physical, biological, or chemical indications of instability or deterioration

1.2.3.7 The source and measure of the IVDs activity must be indicated on the container;

1.2.3.8 The storage instructions adequate to protect the stability of the product must be clearly indicated (i.e., temperature, humidity, etc.)

1.2.3.9 There must be instructions for manipulation of products requiring mixing or reconstitution, along with instructions for storage of products that have been reconstituted or mixed;

1.2.3.10 There must be a means to assure that the product meets appropriate standards of purity, quality, etc., at the time of use, including one or more of the following:

- expiration date (date beyond which the product is not to be used);
- statement of any visual indication of alteration;
- instructions for a simple check to assure product usefulness;
- The net quantity of contents.

1.2.4 Instruments:

1.2.4.1 The use and function of the instrument must be stated;
1.2.4.2 There must be an instruction manual for installation and use
1.2.4.3 The performance characteristics and specifications of the instrument must be indicated;
1.2.4.4 The calibration procedure must be indicated;
1.2.4.5 All operational precautions and limitations must be indicated;
1.2.4.6 The symbols associated with various hazards must be indicated;
1.2.4.7 There must be information on service and maintenance of the equipment.

1.2.5 Inserts

Labeling must contain in one place the following information in the format and order listed below, except where information is not applicable, or as specified in a standard for a particular product class;

1.2.5.1
1.2.5.2 If the IVD is a reagent intended as a replacement in a diagnostic system, labeling may be limited to that information necessary to adequately identify the reagent and to describe its use in the system;

1.2.5.3 If the IVD is a multiple purpose instrument used for diagnostic purposes, and not committed to specific diagnostic procedures or systems, labeling can be restricted to the following:

- The proprietary and established product name;
- The intended use of the product and whether it is a qualitative or quantitative type of procedure;
- Summary and explanation of the test, including a short history containing methodology and the special merits and limitations of the test;
- The chemical, physical, physiological, or biological principles of the procedure.

1.3 Specimen Collection and Preparation for Analysis

It is also required that specimen collection and preparation for analysis must describe:

1.3.1 Special precautions/preparations;
1.3.2 Additives necessary to maintain specimen integrity;
1.3.3 Known interfering substances; and
1.3.4 Recommended specimen storage and handling instructions.
1.3.5 A step-by-step outline of recommended procedures from the reception of the specimen to the obtaining of results;
1.3.6 In addition to the following, there should be a list of any points that might improve precision or accuracy; such lists include"

- A list of materials provided and instruction for use, e.g., reagents, equipment;
- A list of necessary materials that are not provided (include details such as sizes, numbers, types and quality;
- A description of the amounts of reagents necessary, and parameters such as time, temperature, etc.;
- A statement related to final reaction stability and any time restrictions on accurate measurements;
- Details of calibration, identifying and listing and necessary preparation of the reference materials, samples, and blank;
- Description of the calibration range including the highest and lowest values measured;
- Details of necessary quality control procedures and materials, e.g., positive and negative controls, acceptable performance limits;
- Explanation of the procedure for calculating the unknown, including the definition of each component of the formula, a sample calculation, and the number of significant figures appropriate for the answer;
- Limitations of the procedure, e.g., identify situations which will have an adverse impact on test results. If further testing either more specific or more sensitive, is indicated in all cases where certain results are obtained, the need for the additional test shall be stated;
- Expected values including how the range(s) was established and identify the populations on which it was established;
- Specific performance characteristics as appropriate including accuracy, specificity, precision, and sensitivity;
- References;
- Name and place of business of the manufacturer, packer, or distributor;
- Date of issuance of the last labeling revision by the firm.

1.4 Exemptions from Labeling Requirements

1.4.1 A shipment or delivery for an investigation subject, Investigational Device Exemption (IDE), if the device is in compliance with the subject IDE;

1.4.2 A product in the laboratory research phase, not represented as an IVD that is prominently labeled: "For Research Use Only. Not for use in diagnostic procedures;"

1.4.3 A product that is being shipped or delivered for testing prior to full commercial marketing that is prominently labeled: "For Investigational Use Only. The performance characteristics of this product have not been established."

CHAPTER 2

REPACKAGING AND RELABELLING OF IN-VITRO DIAGNOSTICS

2.1 Packaging Material

In accordance with the methods of use and administration of IVDs, packaging materials, closures and containers vary a great deal and have to meet a wide variety of different requirements.

2.1.1 The manufacturer should include in the product information supplied to the re-packager specifications about the packaging materials as approved in the original application or in the amended original application for registration including its oxygen and light transmission characteristics in order to enable the re-packager to properly select an equivalent container–closure system.

2.1.2 A re-packager may or may not use the same container-closure system as the manufacturer.

2.1.3 If the container-closure system is different, the re-packager should use a container–closure system that is at least as protective as, or more protective than, the original container–closure system in terms of moisture vapour transmission rate (MVTR), oxygen transmission, light transmission, and compatibility of the container–closure system with the medicine (equivalent container-closure system).

2.1.4 System equivalency extends to any special protective materials, such as for light transmission, seals, or desiccants associated with the original container–closure system.

2.1.5 These values may be determined by the re-packager, or they may be obtained from the container–closure vendor for the specific container– closure system under consideration.

2.2 Bulk Products

The following criteria should be considered by the re-packager upon receipt of bulk prior to repackaging:

2.2.1 The bulk product should be distributed to the re-packager by the manufacturer in accordance with the requirements for distribution as contained in this Guideline and accompanied by appropriate labelling, batch numbers and valid expiry date. The re-packager should also receive Material Safety Datasheet, Certificate of Analysis, and sample market labelling including product information inserts from the IVD manufacturer.

2.2.2 The bulk product should be received intact and undamaged and in appropriately labelled containers.

2.2.3 The bulk product should undergo definitive organoleptic evaluations to confirm its identity (e.g. physical appearance, marking/s, colour, and odour) to confirm the labeling as

described by the manufacturer.

2.2.4 Records should be maintained to verify the identity and quantity of each shipment received and to verify the batch number and bar coded information for each article shipment received. These records should also include the name of the manufacturer or supplier and the date of receipt.

2.2.5 The re-packager should store and maintain the bulk under storage conditions specified by the manufacturer.

2.3 Repackaging Process

The following criteria should be observed:

2.3.1 The re-packager operations should be conducted under specified storage conditions as instructed by manufacturer and that includes maintenance of required temperature in areas where repackaging is conducted.

2.3.2 The re-packager must ensure that all information provided by the manufacturer has been affixed on the secondary packaging.

2.3.3 Written procedures should be in place and maintained to ensure that correct packaging materials are used for the repacked IVDs and required conditions are met.

2.3.4 ***Establishing an expiry date***. To establish the expiry date, stability studies are performed on the IVD in the original manufacturer‘s package system. When an IVD is repackaged into a different container, its expiry date may be altered or interrupted.

2.3.5 The re-packager may perform stability studies on the repacked IVDs to establish an expiry date for the repackaged product based on scientific evaluation of the medicine in the equivalent container–closure system and complies with criteria established for equivalency.

2.3.6 **Establishing equivalency** means the following:

- The requirements stated in this guideline are met.
- Specifications such as light transmission, seals or desiccants associated with the original container–closure system, or special protective materials in which the IVD is marketed, are the same. Comparison of container–closure systems may be done through stress testing of the product after storage under exaggerated conditions of temperature and humidity.
- A re-packager should not use the equivalent container-closure system criteria to repackage IVDs where such products have been identified by the manufacturer to have stability problems or if the manufacturer specifically states that the product should not be repackaged using the equivalency container closure-system criteria. For e.g. the IVD is labile (moisture sensitive) and therefore should be dispensed only in the original manufacturer‘s container. In this case, a re-packager needs to demonstrate the stability of the medicine in the re- packager‘s container closure system.

CHAPTER 3

REQUIREMENTS FOR DISTRIBUTION OF IN-VITRO DIAGNOSTICS

3.1 General Requirements

3.1.1 Personnel

Support Staff must be adequately trained in quality assurance, safety, good storage practice, and regulatory procedures and shall observe a high level of personal hygiene and sanitation

3.1.2 Premises and Facilities (Storage Areas)

Receiving and Dispatch Bay: Reception and dispatch areas must be designed and equipped to facilitate protection of products from the weather as well as cleaning before storage.

Accessibility to Storage Area: Precautions must be taken to prevent unauthorized persons from entering storage and restricted areas.

Size and Capacity: The size and capacity of a storage area must be of sufficient capacity to allow for the orderly storage of products. IVDs must be orderly arranged to facilitate cleaning and inspection. Pellets, racks, shelves and other packing aids shall be kept in a good state of cleanliness and repair

Storage Areas: Storage areas must be clean, dry, and free from accumulated waste and vermin.

Pest Control: There shall be a written programme for pest control which shall be adhered to.

Ventilation and Illumination: There must be adequate ventilation and lighting.

Dispatch and Transport: IVDs must be transported in such a way that their integrity is not impaired and that storage conditions are maintained.

3.2 Specific Requirements

3.2.1 Storage Requirements:

Appropriateness of Storage Conditions: An IVD shall be stored in consonance with storage conditions on the label.

Monitoring of Storage Conditions: Where special storage condition is required, an appropriate temperature monitoring data must be kept for inspection.

Temperature Monitoring: Temperature mapping of the storage facility must show uniformity of temperature throughout the facility.

Equipment Calibration: Equipment for monitoring temperature and relative humidity conditions of the facility must be calibrated at defined intervals.

3.2.2 Management of IVDs:

- IVDs must be stored in such a manner as to prevent contamination, mix-ups and cross-contamination.

- Stocks must be appropriately rotated. The " first expired - first out " and "first in - first out " principles must be followed.
- Products must be controlled under a quarantine system designed to prevent their use until a final decision has been taken.
- Broken or damaged items must be withdrawn from wholesome stock and separated.

3.2.3 Documentation:

Written instructions, procedures and records shall be kept up to date on the premises of the storage facility. These shall include, but not be limited to, the following: (i) Delivery (ii) Storage (iii) Stock rotation and control (iv) Expired stocks handling (v) Returned or recalled goods handling (vi) Cleaning (vii) Pest control

CHAPTER FOUR

SANCTIONS

4.1. Sanctions

A person who contravenes a provision of these Guidelines is guilty of an offence and liable on conviction:

4.1.1. In case of an individual, to imprisonment for a term not exceeding two years or to a fine not exceeding L$50,000.00 or to both fine and imprisonment; and

4.1.2. In case of a body corporate, to a fine not exceeding L$100,000.00

4.1.3. Where an offence under these Regulations is committed by a body corporate or firm or other association of individuals:

- Every director, manager, secretary or other similar officer of the body corporate; or
- Every partner or officer of the firm; or
- Every trustee of the body concerned; or
- Every person concerned in the management of the affairs of the association; or
- Every person who was purporting to act in a capacity referred to in this regulation, are severally guilty of that offence and liable to be proceeded against and punished for that offence in the same manner as if they had themselves committed the offence unless they prove that the act or omission constituting the offence took place without their knowledge, consent or connivance.

4.1.4. Forfeiture: In addition to the penalty specified above, a person convicted of an offence under these regulations shall forfeit to the Authority the IVD product and whatsoever is used in connection with the commission of the offence.

Document History

Summary of Revision	Rationale for Revision
Rev 01	
New Edition	