REPUBLIC OF LIBERIA

LIBERIA MEDICINES & HEALTH PRODUCTS REGULATORY AUTHORITY (LMHRA)

VP Road, Old Road, Oldest Congo Town

Monrovia, Liberia

GUIDELINES FOR REGISTRATION OF MEDICINES AND HEALTH PRODUCTS IN LIBERIA

INTRODUCTION

The regulation of medicines and related health products in Liberia is governed by the provisions and requirements of the Liberia Medicines and Health Products Regulatory Authority (LMHRA) Act, 2010.

The law requires that all medicines manufactured, imported or exported, distributed, or sold in Liberia should be of acceptable quality, safety and efficacy. The process of medicine registration forms an important basis for evaluating and assuring medicines and health products for safety, efficacy and quality.

For products that are registered by the West Africa health Organization (WAHO) for region wide use, the LMHRA shall cause it to be registered upon receipt of summary decision by WAHO and the payment of the applicable fees by the applicant. Applications submitted for registration in the WAHO Common Technical Document (CTD) format shall be accepted for processing.

LEGAL BASIS

In pursuance of Part 1 Section 1 of the Act to Establish the Liberia Medicines and Health Products Regulatory Authority (LMHRA) of 2010, these guidelines are hereby made to provide guidance to applicants on the procedure for registering medicines and health products in Liberia. Applicants are required to familiarize themselves with this document and the above law before completing the registration application form (Appendix 1)

INTERPRETATION

In these guidelines, unless the context otherwise states: -

a) "**Authority**" means Liberia medicines and Health Products regulatory Authority

b) **Applicant**: Means a person, manufacturer or company who submits application for registration of medicine and health product to the Authority; and responsible for compilation of information for registration

c) "**allopathic drug**" means - any product or substance other than a medical device, which is to be administered to one or more human beings on its own, or as an ingredient in the preparation of a substance, for a medicinal purpose.

d) "**medicinal purpose**" means - use for treating or preventing a disease, diagnosing or ascertaining the presence and extent of a physiological function, contraception, inducing anaesthesia, altering normal physiologic function permanently or temporarily in any way in humans.

e) "**variation**" means - a change in the indication(s), dosage recommendation(s), drug classification and/or patient group(s) for a previously registered drug being marketed under the same name in Liberia. A variation also includes, but is not limited to, a change in the product name, site of manufacture and/or source of ingredients.

f) "**new chemical entity**" means - a chemical or biologically Active Pharmaceutical Ingredient (API) that has not previously been issued with a marketing authorization as an ingredient of any pharmaceutical product in Liberia

g) "**lead market brand**" means- a proprietary or branded generic product which has been determined by criteria including but not limited to the following:
   - sales volume
   - safety profile
   - number of prescriptions
   - expert opinion

   and so declared by the Liberia Medicines and Health Products Regulatory Committee

h) **"International Non-proprietary Name (INN)"** means the approved chemical name of the product.

i) "Innovator drug" means - a drug for which a New Drug Application (NDA) has been submitted to a regulatory authority and marketing authorisation granted.

j) "Generic drug" means a finished product based on an active substance which is marketed under a different name from that of the original branded medicinal product or under its common name..

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k) **Active Ingredient:** Means a substance with a therapeutic, diagnostic or prophylactic activity used in a pharmaceutical product. Drug Substance" and "Active Substance" are synonymous to "Active Ingredient."

l) **Closure:** Means a part of the container.

m) **Container:** Is that which holds the article and is or may be in direct contact with the drug.

n) **Dosage Form**: Formulation of an active ingredient(s) so that it can be administered to a patient in specified quantity/strength eg. tablets, capsules, injection solution, syrups, ointments, suppositories, etc. "Pharmaceutical Form" and "Finished Product" are synonymous to "Dosage Form."

o) **Counterfeit Medicine:** Means a medicine that is deliberately and fraudulently mislabelled with respect to identity for source. Counterfeit products may be branded or generic medicines, and may include products with the correct ingredients, with the wrong ingredient, without ingredients, with insufficient active ingredient, or with fake packaging material.

p) **Immediate or Primary Container:** Is that part of container which is in direct contact with the medicine at all times

q) **Labeling: Includes any legend,** word or mark attached to, included in, belonging to or accompanying any medicine including: 1) The immediate container label 2) Cartons, wrappers and similar items, 3) Information materials such as instructional brochures and package inserts.

r) **Manufacture (Manufacturing):** All operations of purchase of materials and products, production, quality control, release, storage, shipment of finished products and the related controls.

s) **Manufacturer:** A company that carries out at least one step of manufacture.

t) **Medical Device**: Means an instrument that is not a medicine, as defined herein, that is intended for use in the diagnosis, treatment, mitigation or prevention of a disease, disorder, abnormal physical or mental state, or symptoms thereof, in human or animal, or restoring, correcting, or beneficial modification of organic or mental functions in human or animal.

u) **Medical Supply**: Means article that is intended for diagnosis, treatment, mitigation or prevention of a disease, disorder, abnormal physical or mental state, or symptoms thereof, in human or animal or restoring, correcting or beneficial modification of organic or mental functions in human or animal. This includes suturing materials, syringes, needles, bandages, gauze, cotton, artificial teeth, chemicals, and x-ray film and other similar articles.

v) **Medicine:** Means any substance or mixture of substances intended for use in:
(i) the diagnosis, treatment, mitigation or prevention of a disease, disorder, abnormal physical or mental state, or the symptoms thereof, in man or animal; or,

(ii) restoring, correcting or beneficial modification of organic or mental functions in man or animal; or,

(iii) medicine shall include traditional medicine, narcotic drugs, psychotropic substances, blood and blood products, vaccines, sera, and radiopharmaceuticals, but not health products as defined herein.

w) **Pharmaceutical Importer:** Means a registered entity and licensed by LMHRA to procure and import medicines and health products from foreign countries and/or distribution in the commerce of Liberia

REGISTRATION

2.1 NEW APPLICATION

An application for the registration of a drug, either locally manufactured or imported, shall be made in writing as specified in the Application Form

The Application Form shall be completed in accordance with the sequence of appendices and shall be dated, signed and stamped by the applicant/license holder.

Every applicant who is not resident in Liberia shall appoint a local responsible person who must be a person residing or a company incorporated in Liberia and authorized by LMHRA to deal in medicine and Health Products. Evidence shall be made by submitting a power of attorney that

complies with Liberia laws and accompanied with duly signed agreement between the local representative and manufacturers of the finished product. The list of products under the agreement should be appended to the agency agreement.

The local responsible person shall be responsible for facilitating communication with the applicant and when the product is registered he shall assume all legal responsibilities regarding the product safety, efficacy and quality follow-up on the Liberian market.

Applications shall be accompanied by:

a) a duly signed covering letter
b) two (2) completed application forms
c) samples of the product in the final package as specified in Samples Schedule
d) reference or working standard for Active Pharmaceutical Ingredient and related impurities where necessary.
e) all supporting documents as specified on the application form
f) clinical trial and/or bioequivalence trial certificate where applicable
g) non-refundable application fee as specified in Fee Schedule

The Authority shall approve the application before any importation of the product, other than those used as samples for the purpose of this application, shall be made into the country.

REGISTRATION VARIATION

An application for a variation of the registration of a product prior to its re-registration becoming due may be made to the Authority.

The application shall be accompanied by:

a) a duly signed covering letter
b) documentation in support of the variation
c) samples reflecting the variation as specified in the Samples Schedule.
d) a non-refundable variation fee as specified in the Fee Schedule

This variation shall be approved by the Authority before any importation of the varied product, other than those used as samples for the purpose of this application, shall be made into the country.

RE-REGISTRATION

2.3.1 An application for the re-registration of a drug shall be made three (3) months before expiration of the last registration.

The application shall be accompanied by:

a) **a covering letter**
b) **supporting documentation for any variations since the product was last registered**
c) **samples of the product in the final package as specified in the Samples Schedule.**
d) **a non-refundable application fee as specified in Fee Schedule**

The re-registration shall be approved by the Authority before any importation of the product, other those used as samples for the purpose of this application, shall be made into the country.

GENERAL REQUIREMENTS

3.1 SAMPLES

3.1.1 The presentation of the product shall not have any resemblance in spelling and pronunciation of name or packaging to another product that has been previously registered by the Authority.

All samples of oral liquid preparations (solutions, suspensions, syrups) shall have an appropriate graduated plastic measure included in the final package; for antibiotics and other medicaments which require eight hourly administration, a minimum of 75 ml volume is imperative.

All samples submitted shall conform to labeling regulations in force in Liberia

3.1.4 The use of an International Non-proprietary Name (INN) as a brand shall not be permitted.

The brand name of the product shall not have any resemblance in spelling and pronunciation to the INN.

General labeling requirement;

Each product should be accompanied with appropriate labeling including package insert and immediate container labeling.

All label statements required by regulation should be in English.

The label should not be described or presented in a manner that is false, misleading or deceptive or is likely to create an erroneous impression regarding its use in any respect either pictorially or in words.

Statement required to appear on the label should be clear, prominent, indelible and readily legible by the consumer under normal conditions of purchase and use.

Minimum required information for labeling

- Name of product
- Dosage form
- Indication and recommended dosage of the product
- Mode of administration
- Duration of use
- Major adverse effects, if any
- Symptoms and management of overdose
- Contraindication, warning, precautions and major drug interactions
- Use during pregnancy and lactation
- Expiry date
- Batch number
- Shelf life and storage condition
- Name of manufacturer and/or applicant with full location address

3.2 NEW CHEMICAL ENTITIES OR INNOVATOR PRODUCTS

3.2.1 Registration in Liberia shall normally not be permitted within the first two years of the first registration of the drug on the international market.

3.2.2 Verifiable information shall be provided regarding the date of expiry of the patent.

3.2.3 Although clinical trial data derived from studies in other countries will be considered in taking a decision with any application, the Authority reserves the right to request for local clinical evaluation, based on existing guidelines for clinical trials, where necessary. The cost of this trial shall be borne by the applicant.

3.3. GENERIC DRUGS

3.3.1. Shall not be marketed in a name similar in pronunciation or form to the innovator product.

3.3.2. A bio-equivalence study report shall be submitted in line with existing guidelines WHO Guidelines

3.3.3. Although bio-equivalence data derived from studies in other countries will be considered in taking a decision with any application, the Authority reserves the right to request for local clinical evaluation, based on existing WHO guidelines for bio-equivalence studies, where necessary. The cost of this trial shall be borne by the applicant.

For all solid oral dosage forms, reports of dissolution studies will be required. If the official compendia monograph doesn't require dissolution the dissolution requirement in the USP shall apply.
If the product is manufactured on contract basis, evidence of the contract shall be submitted. This information shall be clearly stated on the product label and package insert.

For both locally manufactured and imported drugs the original certificate of analysis for the drug, issued by a recognized public analyst, shall be submitted.

For imported drugs a Certificate of Pharmaceutical Product (CPP) issued by the statutory national drug regulatory authority, in accordance with the World Health Organization (WHO) Certification Scheme for Pharmaceutical Products Moving in International Commerce, shall be submitted along with the certificate of analysis.

If the product is not identical to that in the issuing country, the applicants must list any differences in the application form and justify the differences. The Authority will decide whether the differences are minor and have been adequately justified, and consequently whether certificate is relevant for the intended purposes.

Where different phases of the manufacturing are conducted in different countries, the CPP must be issued by the competent authorities in the country that directly exports the product to Liberia. Different phases of manufacture may be conducted in different countries.

Where the product is fully manufactured in both in different countries and the applicant wishes to obtain approval to use both sites of manufacture, the certificate should be submitted from both countries.

The certificate should officially be stamped and dated together with all copies of product information submitted in support of an application for registration.

The applicant is responsible for providing a notarized translation of the contents of the certificate in English in case when the certifying Authority issued the certificate in any other language.

The certificate should be original and/or a notarized or certified copy and current.
A Drug Master File and process validation protocols shall be submitted for all applications.

Stability study reports conducted for three (3) trial batches of the product, and suited to the conditions specified below, shall be submitted :-

a) WHO Zone IV climatic conditions

Condition	**Accelerated**	**Real Time**
Storage Temperature	40 $\pm$ 2 ^{o}C	30 ^{o}C
Relative Humidity	75 $\pm$ 5 %	70 +/- 5 %
Duration	6 months	Until end of shelf life

b) The stability study shall be conducted in the container closure system in which the product will be marketed in Liberia.

Where the product is to be registered in more than one container closure system, stability data shall be provided for each presentation. Real-time stability data shall be required for all biologicals.

The result of the stability test shall be presented in both tabular and graphical forms and the proposed shelf-life and storage conditions shall be determined on the basis of these results.

The Authority in considering an application:

a) shall satisfy itself that there is need to have the drug registered in Liberia.

b) shall request the applicant to submit a manufacturer's authorization to register the drug.

c) may consult with other bodies and experts with knowledge of the drug.
d) For purposes of verification of compliance to cGMP, all applications shall be accompanied by a Site Master File.

e) Reserves the right to conduct a Good Manufacturing Practice (GMP) audit inspection on the manufacturing facility for the product at a fee prescribed by the Authority.

f) May ask the applicant to supply such other information as may be required to enable it reach a decision on the application.

g) Shall acknowledge receipt of all applications at submission and payment of fees and shall be processed within three months. Where it becomes necessary to ask for additional information from the applicant, this time period may be lengthened.

h) When the applicant fails to submit written responses to queries within 6 months from the date of their issuance, it will be deemed that the applicant has withdrawn the application or if the queries have been reissued for a second time and the applicant provides unsatisfactory responses, the product will be disqualified and the application will be rejected. The applicant will be required to apply afresh.

i) If no response is received within six months of the request, the application will be discontinued.
j) Decisions on registration shall be based on the dossier evaluation report, quality control report and inspection report on compliance to cGMP where necessary.

An appeal for the review of an application may be made in writing to the Chairman of the LMHRA within thirty (30) days of receipt of the rejection notice.

Where the Authority is satisfied that there is the need to register a medicinal product, and all requirements for its registration have been satisfied, it shall do so and issue to the applicant a certificate of registration, subject to such conditions as may be prescribed by the Authority from time to time.

The registration of a drug under these regulations, unless otherwise revoked, shall be valid for a period of three (3) years and may be renewed.

The Authority shall from time to time, publish a notice in the Gazzette notifying the registration of a drug under these regulations.

No information given in this application shall be disclosed by the LMHRA to a third party except:-

a) with the written consent of the license holder; or

b) in accordance with the directive of the Board of Directors of LMHRA or

c) for the purpose of a legal process under the LMHRA Act of 2010

The Authority shall cancel, suspend, or withdraw the registration of a drug if:-

a) the grounds on which the drug was registered is later found to be false; or

b) the circumstances under which the drug was registered no longer exist; or

c) any of the provisions under which the drug was registered has been contravened; or

d) the standard of quality, safety and efficacy, as prescribed in the documentation for registration is not being complied with; or

e) the premises, in which the drug or part thereof is manufactured, packaged or stored by or on behalf of the holder of the certificate of registration is unsuitable for the manufacture, packaging or storage of the drug.

Where the registration of a drug is suspended, withdrawn or cancelled, the Authority shall cause the withdrawal from circulation of that drug and shall accordingly cause the suspension, cancellation or withdrawal to be published in the Gazzette

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