RWANDA FDA
Rwanda Food and Drugs Authority

GUIDELINES ON SUBMISSION OF DOCUMENTATION FOR REGISTRATION OF HERBAL MEDICINAL PRODUCTS FOR HUMAN USE

FEBRUARY 2023

FOREWORD

Rwanda Food and Drugs Authority (Rwanda FDA) 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 herbal medicinal products in order to protect public health by increasing access and availability of essential medicines.

Considering the provisions of the regulations No. DFAR/HMDAR/TRG/001 Rev.3 governing the registration of Human Medicinal Products especially in its articles 2, 5, 6,7,8, 9, 10 and 11, the authority has issued these *Guidelines No DFAR/HMDAR/GDL/015 on Submission of Documentation for Registration of Herbal Medicinal Products for Human Use.*

These guidelines have been developed to provide guidance to the applicants on the requirements to be fulfilled for herbal medicinal products marketing authorization and the document assists the Authority in evaluation of compliance with the set requirements for registration of herbal medicinal products.

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

Dr. Emile BIENVENU
Director General

GUIDELINES DEVELOPMENT HISTORY

DRAFT ZERO	**28/03/2022**
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STAKEHOLDERS CONSULTATION	**27/07/2022**
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DOCUMENT REVISION HISTORY

Date of revision	Revision number	Changes made and/or reasons for revision
09/02/2023	0	Fist Issue

TABLE OF CONTENTS

ACCRONYMES AND ABBREVIATIONS

LTR: Local Technical Representative
GMP: Good Manufacturing Practices
CoAs: Certificates of Analysis

GLOSSARY / DEFINITIONS

In these guidelines, unless the context otherwise states:

"Authority" means Rwanda Food and Drugs Authority or its acronym "Rwanda FDA".

"Herbal Medicinal Product" means any finished labelled medicinal product that contains active ingredients, aerial or underground parts of the plant or other plant material or combination used for the purposes of treatment or prevention of a disease or altering normal physiological function, permanently or temporarily in any way in humans.
Or
includes plant-derived material preparations with therapeutic or any other human health benefits which contain raw or processed ingredients from one or more plants and materials of organic or animal origin.

"Herbal Material" means whole, fragmented or cut (including chopped) plant, part of plants (including leaves, roots, flowers, seeds, bark, fresh juices, gums etc) in an unprocessed state usually in dried form. For the purposes of this guidance document, herbal powders (herbal materials that are dried and ground to powders) are also included in this definition.

"Herbal Preparations" include comminuted or powdered herbal materials, or extracts, tinctures and fatty oils of herbal materials.

"Applicant" means the product owner or Marketing Authorization Holder. Representatives of Marketing Authorization Holders may not hold themselves as applicants unless they own the product.

"Active Herbal Ingredient, or Drug Substance" means herbal material or herbal preparation with required therapeutic activity.

"Batch or Lot" in relation to herbal medicinal product means a defined quantity of herbal medicinal product manufactured in a single manufacturing cycle and which has homogeneous properties.

"Composition" means the ingredients of which the herbal medicinal product consists, proportions, degree of strength, quality and purity in which those ingredients are contained.

"Container" means bottle, box, packet or sachet which contains or is to contain herbal medicinal product.

"Country of Origin" means a country in which the herbal medicinal product has been manufactured.

"Dosage Form" means the form in which herbal medicinal product is presented, e.g tablet, capsule, elixir, powder etc.

"Dossier" means file(s) containing detailed technical information of a particular herbal medicinal product.

"Excipient" means any component of a finished dosage form other than active herbal ingredient which has no therapeutic value.

"Label" means any tag, brand, mark, pictorial or other descriptive matter, written, printed, stencilled, marked, embossed or impressed on or attached to a container of any herbal medicinal product.

"Manufacture" means and includes all operations involved in the production, preparation, processing, extraction, compounding, formulating, filling, refining, transforming, packing, packaging, re-packaging and labelling of herbal medicinal product.

"Manufacturer" means a person or firm that is engaged in the manufacture of herbal medicinal product.

"Shelf Life" means that length of time in which the herbal medicinal product is given before it is considered unsuitable for sale or consumption or it is amount of time that a properly packaged and stored product will last before undergoing chemical or physical changes, remaining within the specified uncertainty.

"Specification" means list of tests, references to analytical procedures and appropriate acceptance criteria which are numerical limits, ranges or other criteria for the tests described.

"Local Technical Representative (LTR)" Any applicant who is not resident in Rwanda shall appoint a local technical representative who must be a company incorporated in Rwanda and authorized by Rwanda FDA to deal in medicinal products and must hold a wholesale operating license. The appointment shall be notified to the Authority by submitting a letter of appointment supported by original copy of power of attorney duly notarised in country of origin, and registered with registrar of Companies in Rwanda.

"Marketing Authorization (Registration Certificate)" Approval from the Authority necessary to market and sell a product in Country. This is a legal document that establishes the detailed composition and formulation of the product and the pharmacopoeia or other recognized specifications of its ingredients and of the final product itself, and includes details of packaging, labelling and shelf-life.

"Mock Ups" A copy of the flat artwork designed in full colour, providing a replica of the outer and immediate packaging, providing a two dimensional presentation of the packaging or labelling of the herbal medicinal product. It also refers to as a paper copy or computer generated version.

I. INTRODUCTION

Pursuant to the provisions of the Law N° 003/2018 of 09/02/2018, establishing Rwanda FDA, determining its mission, organization and functioning especially in its articles 3, 8 and 9;

Pursuant to the provisions of the Regulations No *DFAR/HMDAR/TRG/001* governing the registration of medicinal products especially in its articles 2, 5, 6,7,8, 9, 10 and 11, the Authority has issued *Guidelines No DFAR/HMDAR/GDL/015 on Submission of Documentation for Registration of Herbal Medicinal Products for Human Use.*

II. SCOPE

These guidelines apply to product dossier applications for herbal medicinal products intended for human use and provide guidance to the applicants on the requirements to be submitted to the Authority for marketing authorization.

III. REQUIREMENTS

Each application should include the general, specific and quality requirements as outlined below:

III.1 General requirements

III.1.1 Preparation of the product dossier application

The applicant shall prepare and present the product dossier application information according to the following requirements:

a) The application should be typed in either **English, French or Kinyarwanda.**
b) The application must contain a complete index to the various appendices.
c) All pages of the application should be numbered in the style: ***page x of y (e.g. page 1 of 30).***
d) Payment of fees shall be made in accordance to regulation N° CBD/TRG/004 related to regulatory services tariffs/ fees and fines. The fees are for each respective product registration excluding transfer and other charges.
e) The PDF documents should be in OCR (Optical Character Recognition), selectable and searchable.

III.1.2 Submission of application

An application for product registration for either locally manufactured or imported, shall be made in writing using a cover letter No DFAR/HMDAR/FMT/024 and application form No. DFAR/HMDAR/FOM/025 downloadable from Rwanda FDA website www.rwandafda.gov.rw , dated and signed by the applicant.

If the applicant is a foreign company, the applicant shall appoint a local technical representative through whom an application shall be submitted. The local technical representative shall be a registered pharmaceutical/herbal medicinal products wholesale company or an accredited manufacturer's representative.

The application should be submitted to Rwanda FDA through the authorized local technical representative to the following address:

Director General
Rwanda Food and Drugs Authority
P. O. Box 1948, Kigali- Rwanda
NYARUTARAMA PLAZA, RWANDA
KG 9 Avenue Kigali
Email: info@rwandafda.gov.rw

For the purposes of submission of Product Dossier to Rwanda FDA, an application for registration of product that is intended to be placed on the Rwandan market for the first time shall include the following:

a) Signed and dated original hard-copy of cover letter
b) Signed and dated application form for herbal medicinal product registration
c) Complete documentation as per these guidelines supported by reports with data on quality, safety and efficacy.
d) Proof of payment of registration fee at the time of submission.
e) Non-refundable GMP inspection fee as stipulated in the regulation N° CBD/TRG/004 related to regulatory services tariffs/ fees and fines.
f) Two CD-ROMs containing product dossier administrative and technical information in searchable (PDF). The application form should be in MS-Word.
g) Two commercial samples of the herbal medicinal product with Certificates of Analysis.

III.2 Specific requirements

a) 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 Rwanda FDA.
b) All samples submitted should conform to existing Rwanda FDA guidance No DAR/GDL/010B on format and content of labels for human medicinal products.
c) Patient Information Leaflets for all submitted samples should conform to existing Rwanda FDA guidance No DAR/GDL/010C on format and content of Patient Information Leaflets for human medicinal products.
d) Scientific and/or botanical names of the plants used, as well as the parts of plants used and the quantity of active herbal ingredients used in the preparation, shall be submitted.
e) The list of all excipients used and their quantities per dosage units used in the preparation shall be submitted.
f) The indications for which the herbal medicinal product is being presented for registration shall be unambiguously stated.
g) Copies of the leaflet insert and labels mock ups shall be included in the documentation.
h) If the product is produced on contract manufacture, evidence of the contract agreement shall be produced in the documentation submitted.

III.3 Quality requirements

a) In order to ensure quality of the herbal medicinal products, manufacturers should specify and implement quality requirements at every stage of manufacture.
b) A certificate of analysis for each herbal medicinal active ingredient should be provided with detailed information as to the testing performed to confirm the identity and purity of the medicinal ingredient.
c) The finished product specifications must be provided for every herbal medicinal product. The specifications should indicate which tests are carried out routinely on each batch of the herbal

medicinal product, and for those which are not carried out routinely, the frequency of the testing should be stated on the specification sheet.

d) The Product Labelling Information (including package insert) shall meet the following:
The print size and colour should be legible and typed in one of the official languages used in Rwanda. The product label should include the following information:

i. Name of the product
ii. Composition: The quantitative list of main active ingredients including the common name of the relevant plants. If the product is imported, plant name should be mentioned along with botanical name
iii. Dosage form
iv. Pack size
v. Name of manufacturer and physical address of the manufacturing site
vi. Lot/Batch number
vii. Manufacture date and expiry date
viii. Storage conditions

The package insert should contain the following information in one of the official languages:

i. Name and description of the product
ii. Composition
iii. Pharmacological properties, where information is available
iv. Therapeutic indications
v. Dosage: the minimum and maximum as well as average dosage levels, must be stated (if appropriate, specified for children and the elderly).
vi. Contraindications/precautions, Interactions and Cautions/warnings
vii. Name and address of the manufacturer
viii. Overdose and treatment
ix. Adverse reactions
x. Special considerations e.g. vaginal, rectal, and urethral preparations
xi. Storage conditions
xii. Main vehicle/base

e) Stability studies shall be conducted for 3 (three) trial batches of production and the proposed shelf-life and storage conditions must be determined, based on these results.

WHO Zone IVB climatic conditions:

Condition	**Accelerated**	**Real Time**
Storage Temperature	40 ± 2°C	30 ± 2°C
Relative Humidity	75 ± 5%	75 ± 5%
Duration	6 months	Until end of shelf life

f) The above mentioned stability studies shall be conducted in the container closure system in which it will be marketed in Rwanda.
g) Where applicable, a Certificate of Pharmaceutical Product (CPP) in accordance with the WHO Certification scheme/or Free sale certificate and issued by the statutory regulatory

authority in the country of origin of the product, shall be submitted along with a certificate of analysis.

III.3.1 Physical/chemical tests

III.3.1.1 Organoleptic and identity test

Physical identification tests should be done on the final dosage form and should be documented in the herbal medicinal product specifications. Tests for physical identification of the herbal medicinal product might include tests such as organoleptic evaluation (sensory characteristics e.g., taste, odour, feel, appearance (colour and shape of the capsule or tablet, etc.).
Where the active ingredient is a defined chemical entity, or where a marker is present, chemical identification tests should be used.

III.3.1.2 Heavy Metals

Heavy metals such as arsenic (inorganic), cadmium, lead and mercury should be tested individually or as total heavy metals expressed as lead at the herbal medicinal product stage or at the raw material stage if all medicinal and non-medicinal ingredients are tested. Testing should be done according to Pharmacopoeia or any other internationally accepted methods.

III.3.1.3 Pesticide Residues

Testing for pesticides in plant or plant materials, algae, fungi, should be done according to WHO methods for pesticide screening. Multi-residue pesticide screening is preferential. The pesticide residues that are routinely tested should be those pesticides which were used in treatment of the plant or any pesticides where residues are suspected and may carry over to the final dosage form.

III.3.1.4 Foreign matter

Testing should be done according to internationally recognized methods.

III.3.2 Microbial tests

Microbial testing of the under listed parameters should be done according to Pharmacopoeia, WHO methods or any other internationally recognized methods:

a) **Total viable aerobic plate count • Contaminating fungus (yeast and mould)**
b) ***Salmonella* spp**
c) ***Escherichia coli***
d) ***Staphylococcus aureus***

III.3.3 Toxicological Requirements

Acute, chronic and sub-chronic toxicity test reports of the herbal medicinal product shall be submitted.

IV. REGISTRATION TIMELINES

Herbal medicinal product dossiers shall be scheduled for assessment according to (FIFO) basis upon compliance of the requirements. A new application for registration shall be processed within nine **(9)** months (maximum) of receipt of the application. The applicant will be required to provide any requested additional data within ninety **(90)** calendar days. Additional data or query responses shall be processed within sixty **(60)** calendar days.

V. EVIDENCE OF CLAIM

a) Substantial evidence of the clinical effectiveness of the herbal medicinal product for the indications stated shall be required.
b) All indications and claims based on scientific evidence require human studies. For those rare occasions where only non-human data exist, indications and claims may be allowed on a case by-case basis. Supporting evidence may be used in conjunction with primary evidence to strengthen the wording of a claim.
c) In a claim based on scientific evidence, the recommended dosage of the product needs to be consistent with the evidence used to make the claim. The evidence must relate to the whole product or the same active constituent(s) with similar dosage regimen, dosage form and route of administration to the product for which a claim is being made. When the evidence is based on an active constituent, qualification may be necessary according to how other constituents in the product may affect the activity of that constituent in the product.
d) Although foreign clinical data is acceptable, the Authority may request for local clinical trials based on the Authority's Guidelines for Clinical Trials in Humans at its own discretion. The cost of such a trial shall be borne by the applicant.

VI. OTHER CONSIDERATIONS

The Authority, in considering an application:

a) May ask the applicant to supply such other information as may be required to enable it reach a decision on the application.
b) Shall satisfy itself that there is the need to have the herbal medicinal product registered.
c) May rely on other regulatory bodies and experts' opinion with knowledge in the herbal medicinal product.
d) May request for the agreement from the manufacturer to register the herbal medicinal product.
e) May request the applicant to satisfy the Authority that he/she has the resources and facility to execute an effective recall of the product if the need arises.
f) Where the Authority is satisfied that there is the need to register a herbal medicinal product, and all requirements for its registration have been satisfied, it shall issue to the applicant a certificate of registration, subject to such conditions as may be prescribed by the Authority from time to time.

g) The registration of herbal medicinal product under these guidelines, unless otherwise suspended or revoked, shall be valid for a period of 5 (five) years and may be renewed.

h) The Authority shall, from time to time publish the registered herbal medicinal products under these guidelines.

VII. ENDORSEMENT OF THE GUIDELINES

	Author	Checked by		Approved by
Title	**Division Manager**	**Head of Department**	**Quality Assurance Analyst**	**Director General**
Names	Mrs. Clarisse IRASABWA	Dr. Védaste HABYALIMANA	Mr. Théogène NDAYAMBAJE	Dr. Emile BIENVENU
Signature				
Date	13/02/2023	17/02/2023	22/02/2023	24/02/2023

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