THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

TANZANIA FOOD AND DRUGS AUTHORITY

GUIDELINES FOR APPLICATION FOR REGISTRATION OF HERBAL DRUGS IN TANZANIA

(Made under Section 52(1) of the Tanzania Food, Drugs and Cosmetics Act, 2003)

JANAUARY 2004

CONTENTS

ABBREVIATIONS

1.	BP	-	British Pharmacopoeia
2.	EMEA	-	European Medicines Evaluation Agency
3.	GMP	-	Good Manufacturing Practices
4.	ICH	-	International Conference on Harmonization of Registration Requirements of Pharmaceutical Products for Human Use
5.	IP	-	International Pharmacopoeia
6.	Ph.Eur	-	European Pharmacopoeia
7.	RH	-	Relative Humidity
8.	TFDA	-	Tanzania Food and Drugs Authority
9.	TFDCA	-	Tanzania Food, Drugs and Cosmetics Act, 2003
10.	USP	-	United States Pharmacopoeia
11.	VICH	-	International Conference on Harmonization of Registration Requirements of Pharmaceutical Products for Veterinary Use
12.	WHO	-	World Health Organization

FOREWORD

During the last decade, use of herbal drugs has expanded and gained popularity globally. They have not only been used for primary health care of the poor in developing countries but also in countries where conventional drugs are predominant in the national healthcare system.

With the expansion in the use of these drugs worldwide, quality, safety and efficacy have become a challenge to both drug regulatory authorities and the public. These guidelines have been developed to provide requirements in support of quality, safety and efficacy for those who wish to market herbal drugs in Tanzania.

Submission of adequate documentation on quality, safety and efficacy of a herbal drug will enable the Authority to use the information and other factors to assess the suitability of the product for intended use. Applicants are therefore urged to read these guidelines carefully and follow instructions prescribed therein.

I would like to appreciate the contribution of individuals and organization involved in the development of these guidelines. I acknowledge the contribution of the World Health Organization (WHO) and the European Medicinal Products Evaluation Agency (EMEA) whose documents saved as important references in drafting these guidelines. The contribution of all the stakeholders involved in developing these guidelines is highly appreciated. I also extend my appreciation to the TFDA Management in their guidance and provision of resources for developing this important working tool for the Authority.

I am most grateful to the following individuals who worked tirelessly in the preparation of these guidelines: *Mr. L.R. Mhangwa, Dr. C. M. Nshimo, Mr. H. B. Sillo, Dr. P. P. Mhame, Dr. N. B. Chukilizo, Dr. M. J. Moshi, Mr. A. Khea and Ms Rosemary Aaron*. The contribution of all other staff of the Directorate of Product Evaluation and Registration is very much acknowledged. Lastly but not the least, the assistance of *Ms Joyce Komba* for typing and putting the guidelines into the present shape is highly appreciated.

It is anticipated that the guidelines will be revised regularly in response to the experiences gathered from their utilization. We therefore welcome comments and views at any time.

M. Ndomondo - Sigonda
DIRECTOR GENERAL
TANZANIA FOOD AND DRUGS AUTHORITY

INTRODUCTION

The Tanzania Food and Drugs Authority (TFDA) is responsible for ensuring that food, drugs, herbal drugs, medical devices and cosmetics regulated under the Tanzania Food, Drugs and Cosmetics Act (TFDCA), 2003 are safe, effective and of acceptable quality. To this end, section 51 of the TFDCA, 2003 provides that the Authority shall register a herbal drug if it is in the public interest and the product is safe, efficacious and of good quality. In addition, the manufacturing facility should also comply with the minimum requirements for Good Manufacturing Practices (GMP).

The objective of developing these guidelines is to provide requirements for application for marketing authorisation of herbal drugs in Tanzania. It is expected that the guidelines will assist applicants to fulfil the legal requirements for registration of herbal drugs as provided under section 52 of the TFDCA, 2003. This section prohibits manufacture for sale, sell, offer, supply or import of any product regulated under the Act including herbal drugs unless the product is registered.

It is being emphasized that the guidelines address herbal drugs which have undergone standardisation and are manufactured in accordance with GMP from a pharmaceutical industry. They cover products which are adjusted to a defined content of a constituent or a group of substances with scientifically established therapeutic activity, safety and efficacy as specified in category IV of the WHO/AFRO guidelines for registration of herbal medicines.

The guidelines have been divided into six chapters. Chapter I gives various definitions in the context of these guidelines while chapter II provides general requirements on how to file an application, payment of relevant fees and processing of applications. Chapter III provides requirements for summary of product characteristics and chapters IV, V and VI provide guidance on registration requirements for quality, safety and efficacy respectively.

The application form for registration of herbal drugs is provided as an appendix to the guidelines. All applicants will be required to fill in this application form and submit it to the Authority along with other documentation as provided in the guidelines.

CHAPTER I

DEFINITIONS

For the purposes of these guidelines, the following definitions shall apply:

1. **Authority**
   Means, the Tanzania Food and Drugs Authority, or the acronym "TFDA" established under section 4 of the Tanzania Food, Drugs and Cosmetics Act, (TFDCA) 2003.

2. **Active ingredient**
   Means a substance that is intended to be used in the manufacture of a herbal drug as a pharmacologically active substance(s) including plant extracts.

3. **Batch**
   Means a defined quantity of any herbal drug product processed in a single process or series of processes such that it can reasonably be expected to be uniform in character and quality. Batch also means lot

4. **Composition**
   Means the ingredients of a herbal drug which it consists, their proportions and degree of strength.

5. **Container**
   Means a bottle, jar, box, packet, sachet or other receptacle which contains or is to contain in it, and where any such receptacle is or is to be contained in another receptacle, includes the former but does not include the latter receptacle.

6. **Excipients**
   Means a substance, other than active ingredient which has been appropriately evaluated for safety and is included in a herbal drug for specific reason (e.g. preservative, flavourant).

7. **Herbal drug or product**
   Means any labeled preparation in pharmaceutical dosage form that contains as active ingredients one or more substances of natural origin that are derived from plants, which is standardized in terms of constituents and for which therapeutic activity, safety and efficacy are established through scientific studies..

8. ICH countries
Means and include United States of America, Japan and the European Union countries.

9. General sale herbal drug
Means any herbal drug which does not need the direction or prescription by a medical practitioner, a veterinary surgeon or dentist for its use.

10. Label
Means any tag, brand, mark, pictorial or other descriptive matter, written, printed, stenciled, marked, embossed or impressed on or attached to a container of any herbal drug.

11. Manufacture
Includes all operations involved in the production, preparation, processing, compounding, formulating, filling, refining, transformation, packing, packaging, repackaging and labeling of a herbal drug.

12. Manufacturer
Means a person or firm that is engaged in the manufacture of herbal drugs.

13. Markers
Means chemically defined constituents of a herbal drug which are of interest for control purposes independent of whether they have any therapeutic activity or not. Markers may serve to calculate the quantity of herbal drug or preparation in the finished product if that marker has been quantitatively determined in the herbal drug when the starting materials were tested.

14. Pharmaceutical dosage form
Means a form of a completed pharmaceutical product that has undergone all stages of production and quality control including being packaged in its final container and labeled e.g. tablet, capsule, elixir, etc.

15. Pharmacopoeia
Means the current edition of British Pharmacopoeia, European Pharmacopoeia, United States Pharmacopoeia and International Pharmacopoeia.

16. Prescription herbal drug
Means any herbal drug required to be dispensed only upon a prescription given by a medical practitioner, a veterinary surgeon or dentist or any other person approved by the Minister responsible for Health.

17. Specifications

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

18. Standardisation

Means adjusting the herbal drug preparation to a defined content of a constituent or a group of substances with known therapeutic activity respectively by adding excipients or by mixing herbal drugs (e.g standardized extract from pharmacopoeia monograph).

19. Qualified person

Means a person who is knowledgeable in pharmaceutical sciences and entrusted with the responsibility of ensuring that each batch of the finished product aspired for registration is manufactured in accordance with GMP to meet standards prescribed in respect of that herbal drug.

CHAPTER II

GENERAL REQUIREMENTS

All applications shall be made by submitting a dully filled in application form accompanied with prescribed information as prescribed in these guidelines. All documents shall be in Kiswahili or English. However, where original certificates are in another language, copies shall be presented together with certified Kiswahili or English translations.

1. Applicants and responsible persons

(a) Applicant

An application for registration of herbal drugs can be made by owner of the product (an individual, body corporate, partnerships or registered business) responsible for the manufacture or to whose order the product is manufactured for sell in Tanzania.

The applicant shall be responsible for the product, information supplied in support of his application for registration and alterations thereof.

(b) Responsible person

Every applicant who is not resident in Tanzania shall nominate a person who resides in Tanzania to be a responsible person. Every nominee shall submit a power of attorney as evidence of his/her nomination.

The responsible person shall:

(i) Monitor the product on the market and inform the Authority immediately after the detection of any problem relating to a registered product such as serious manufacturing defects which may endanger public health.

(ii) Facilitate communication between the applicant and the Authority on matters relating to the product.

(iii) Handle product recalls according to TFDA established recall procedures.

2. Applications

(a) First time application

A separate application is required for each product, i.e. products containing the same ingredients but made to a different specification (in terms of strength or content of active ingredients, dosage form, etc) or by a different manufacturer.

However, products other than injectables, made by the same manufacturer to the same specifications, strength (content) of ingredients and form, but differing only in packing or pack sizes require only one application.

Applications shall be made by submitting a dully filled in application form which shall be accompanied with:

(i) Complete documentation as per these guidelines supported by independent expert reports on quality, safety and efficacy.

All ingredients must comply with specifications prescribed either in the United States, European, British or International pharmacopoeias. In-house specifications may be acceptable if justified.

(ii) Original Certificate of Pharmaceutical Product (WHO type) from the Drug Regulatory Authority of the country of origin of the product. This shall be accompanied with approved product information.

(iii) Non refundable application fee of US$ 500.00 per product to be imported or US$ 100.00 for products produced locally.

(iv) Non refundable GMP inspection fee of US$ 3000.00 per site for overseas facilities or US$ 100.00 per site for local manufacturers.

(v) Five commercial samples of each package size being applied for registration or sufficient samples to carry out quality control tests as declared in the dossier whichever is higher. The samples must be in the form and container in which they will be marketed.

(vi) An appropriate and complete index/list of the various chapters and documents of the submission.

(vii) Current Site Master File

It should be noted that the above fees may be changed as shall be prescribed under the Fees and Charges Regulations.

(b) Application for alteration of a registered product

Whenever a market authorization holder wishes to make any alteration to a product he must apply to and obtain approval from the Authority in respect of a registered product before introducing it in Tanzania. An application for alteration shall be made on an Application Form for Alteration and shall be accompanied with:

(i) Detailed description of the alteration with supporting reasons.

(ii) Samples of the altered product.

(iii) Non refundable alteration fee of US$ 20.00.

(c) Application for renewal of registration

Applications for renewal of registration of products shall be submitted at least 90 days before the expiry date of registration.

Renewal of registration shall be made on a Renewal Application Form which shall be accompanied with:

(i) Consolidated report of all changes if any (reported and unreported) which had been made with respect to product during the validity of its registration.

(ii) Report of additional adverse drug reactions if any detected during the lifetime of the product.

(iii) Five commercial samples of each package size being applied for registration or sufficient samples to carry out quality control tests as declared in the dossier whichever is higher. The samples must be in the form and container in which it shall marketed.

(iv) Non refundable renewal application fee of US$ 500.00 per product to be imported and US$ 100.00 for products produced locally.

(v) Current site master file.

(vi) Non refundable GMP inspection fee of US$ 3000.00 per overseas manufacturing site and US$ 100.00 per local site.

3. Documentation

(a) Paper type and binding

Data shall be presented on A4 and 80g/m^2 paper with readily readable letters of at least 12 font sizes. Every page shall be numbered sequentially.

Extension sheets, tables, diagrams, and other supporting documents shall as far as possible be of the same size, well-annotated, numbered and appropriately referenced or cross-referenced.

All chapters must be bound separately and arranged sequentially in one or more file covers depending on the number of pages contained in a chapter.

However whenever two or more chapters are bound in a single file, cover marked dividers should separate them. The binding shall be in such a manner as to allow chapters to be detached for evaluation by different experts.

The file cover should be of hard, non-collapsible biodegradable material. Lever arch files and spring files are not permissible. The thickness should be expandable or reducible depending on the total thickness of the contents. The allowable file size is A4 size.

(b) Official references, texts

When direct reference is made to specifications, quality control procedures, test methods, data etc. in official compendia, texts or standard publications other than the current pharmacopoeias, reprints or authenticated copies of relevant pages shall be enclosed. References to pharmacopoeias should specify the year of issue.

(c) Expert reports

Expert reports shall accompany documentation on quality, safety and efficacy. All copies should be authenticated by authorized signatories and stamped officially.

(d) Manuals

An applicant may have several products which are pharmaceutically similar and the same data may be applicable to

these products e.g. specifications for named ingredients, standard analytical methods or test protocols.

In order to avoid unnecessary duplication, this information may be assembled in the form of a manual for e.g. "Manual – Specifications for Ingredients" or Manual – Analytical Methods and Test Protocols".

One hard copy of a manual and a CD-ROM if any should be submitted together with the first application. In subsequent applications appropriate reference may then be made to these "Manuals".

Such manuals must be clearly headed with the company name, title e.g. "Manual – Specifications for Ingredients" and date of compilation. The Authority must be notified of any change of particulars in the manuals.

Binding of manuals should be such as to allow convenient up-dating, revision, additions or removals.

(e) Cross Reference between Products

There shall be no cross reference of particulars or documentation between one product and another (other than reference to above-mentioned "Manuals") except in the following circumstances:

(i) Two or more products in the same pharmaceutical dosage form containing the same active ingredient in different strengths or

(ii) Two or more products in the same pharmaceutical dosage form containing a mixture in different strengths of the same two or more active ingredients in the same proportion.

Separate application forms are required for each such product but supporting documentation if similar, may be cross-referenced provided the application for registration of these products are made at the same time, or within five years of the application for registration of the first product in the group. Appropriate reference must be clearly stated.

4. Submission, payment of fees and processing of applications

(a) Submission of application

All applications shall be addressed and submitted in person or by courier to: *The Director General, Tanzania Food and Drugs Authority, Off Mandela Road, Mabibo External, P. O. Box 77150, Dar es Salaam, Tanzania*

When an application has been received, an acknowledgement will be issued together with a reference number for each product.

(b) Payment of fees

Fees shall be paid either by bank transfer to: *Tanzania Food and Drugs Authority, Account No. 100380013 USD, Citibank, Tanzania Ltd. Dar es Salaam – Head office Peugeot House, 36 Upanga Road, P. O. Box 71625, Dar es Salaam. Swift Code:CITITZTZ. Or Account No.6503900110 National Microfinance Bank, Kariakoo Branch* for local manufacturers.
OR by bankers draft in favour of the Tanzania Food and Drugs Authority. *All bank charges shall be borne by the applicant.*

(c) Processing of applications

Processing of an application shall only be done on complete applications. The Authority may during evaluation of the product request for clarification or additional data or samples and the applicant is obliged to comply. Once a query has been raised, the processing shall halt until after the query has been attended.

The processing of an application takes about 180 days. Immediately after the processing is completed applicants will be informed.

The Authority as part of the evaluation of the product may conduct pre-registration GMP inspection to verify compliance thereof.

5. Registration

When a product is found to have complied with all the prescribed registration requirements, the applicant will be informed to that effect. A certificate of registration together with such conditions as the Authority may determine shall be issued.

A duplicate of the certificate may be issued upon request and on payment of non refundable fee of US$ 20.00.

(a) Validity of registration

The registration of a product shall be valid for five years unless sooner suspended, cancelled or revoked by the Authority or terminated by the registration holder. The validity of registration shall be subject to payment of annual retention fees of US$ 100.00 per product immediately after a product is registered.

(b) Termination of product registration.

The Authority may by giving reasons in writing refuse, suspend, cancel or revoke the registration of a product, or amend the conditions of its registration.

The registration holder may by giving a 60 days written notice and reasons to the Authority terminate the registration of a registered product.

(c) Appeals

Any person aggrieved by a decision of the Authority in relation to any application for registration of a herbal drug may make representations to the Authority, whereby he shall submit information and arguments to convince the Authority to reconsider its decision. However if after reconsideration of the application, the Authority still rejects the application, the applicant may appeal to the Minister for Health.

CHAPTER III

SUMMARY OF PRODUCT CHARACTERISTICS

The following summary of product characteristics shall be submitted for every application:-

1. Trade name and dosage form of the product

2. Physical description of the product

3. Botanical name (Latin Binomial), authority, family of the plant(s) from which the drug(s) has been extracted including plant part(s) used. Synonym if available should also be given. The Kiswahili or English name if available shall be provided. For locally produced products, the local name and tribe.

4. Plant(s) used whether wild or cultivated.

5. Brief pharmacology of the drug

6. Therapeutic indications

7. Dosage regimen and route of administration

8. Brief toxicology of the drug

9. Contraindications

10. Warnings and precautions

11. Drug Interactions

12. Adverse reactions

13. Side effects

14. Shelf life and storage conditions

15. Presentation or pack size(s)

CHAPTER IV

QUALITY REQUIREMENTS

The following information shall be submitted in support of quality of herbal drugs.

1. Brief description of the product.

2. Composition per unit dose

   Give full composition of the preparation including names of active ingredients and excipients, pharmacopoeia reference or in house specifications, reasons for inclusion of each ingredients and quantities per dosage unit.

3. Specification of the starting material(s)

3.1 Give name and address of the supplier of the active ingredient(s) used in the product.

3.2 Submit comprehensive specifications of active ingredients including but not limited to identification tests, tests for foreign matter, total ash, acid insoluble, water extractive matter, particle size, water content, inorganic impurities, toxic metals, microbial limits, mycotoxins, pesticides and fumigation agents, residual solvents and assay. Tests for radioactive residues and sulphated ash may also be done. The test methods should be described in detail.

3.3 Specification of excipients used including those added during the manufacture of the product but not included in the finished product.

4. An outline of the manufacturing procedure for the finished product, including packaging. Enclose a real batch manufacturing record.

5. In process quality control tests

   Details of all control tests including test procedures and limits applied at any intermediate stages of the manufacturing process shall be submitted. These tests are especially required if they cannot be done in the finished product.

6. Specifications of the finished product

   The control tests on the finished product must be such as to allow the qualitative and quantitive determination of the composition of the active ingredient(s).

If a product contains several active ingredients and it is not possible to perform quantitative determination of each active substance the determination may be carried out jointly for several active substances. The need for this procedure must be justified.

Give the specifications of the finished product stating the tests and acceptance criteria. The tests should be described in detail to enable them to be done in any other laboratory. However, if they are pharmacopoeia specifications reference to the relevant pharmacopoeia shall be sufficient provided that a photocopy of the monograph is provided.

Specifications for the finished products shall include:

6.1 Description of the dosage form

6.2 Identification tests for each active substance

6.3 Assay

Validated assays of the content of products along with details of analytical procedure shall be required.

In the case of products containing herbal drugs where the constituents responsible for therapeutic activity are unknown, assays of marker substances or other justified determinations are required.

6.4 Names and levels of impurities including organic and inorganic impurities and residual solvents.

6.5 Microbial limits in which the total count of aerobic micro organisms, the total count of yeasts and moulds, and the absence of specific objectionable bacteria shall be specified. These limits should comply with those in the pharmacopoeia recognized in these guidelines.

6.6 Mycotoxins – The specifications for potential mycotoxins shall be provided and suitable validated methods should be used to control potential mycotoxins.

6.7 Specific tests for dosage forms

6.7.1 Solid dosage forms

The following specific tests shall be done for solid dosage forms (e.g tablets, capsules): dissolution, disintegration, hardness, friability and uniformity of dosage units and water content.

6.7.2 Oral liquids and powders for reconstitution.

The following specific tests shall be done for these dosage forms: uniformity of dosage units, pH, microbial limits, antimicrobial preservative content (where applicable), dissolution (for sparingly soluble products), particle size distribution (for oral suspension), specific gravity, reconstitution time, water content, antioxidant preservative content, extractable volume, alcohol content, redispersibility, and rheological properties.

For specifications which are available in the pharmacopoeia, tests should comply with relevant monograph and copies should be attached.

7. Container and closure system(s)

7.1 Provide detailed description (including liner or wadding) and composition of the packaging material.

Packaging materials for parenteral products shall comply with pharmacopoeia requirements.

7.2 Provide specifications of the packaging material(s).

8. Stability

Applicants are required to provide the stability study report which must include the study design (protocol), type of container, results and conclusions.

The proposed shelf life and storage conditions must be supported by these studies. The shelf life of reconstituted solutions as well as after first opening of sealed containers should also be stated wherever applicable.

Testing must be conducted using containers and closures intended for marketing of the product. For bulk products, testing in prototype containers that simulate the actual packaging is allowed. Information about the type, size and source of containers and closures must be provided to enable determine the expiry period of the product in its container and closure.

Accelerated stability data (6 months) and real time stability studies conducted for a minimum of 12 months should be submitted together with the application. However, studies should continue to the end of the proposed shelf life (a written commitment to this effect should be made by the applicant).

The following are the guides on submission of the Stability data:

INSTRUCTIONS	EXPLANATORY NOTES
8.1. Accelerated stability studies Give brief description of the accelerated stability study conducted to establish the effects of the increase of the rate of chemical degradation and physical change of a drug using exaggerated storage conditions	1. These studies shall be conducted at 40±2°C/75%±5%RH for six months at a sampling frequency of initial, 1, 2, 3, and 6 months in humidity chambers. 2. The parameters to be examined, number of batches, sampling plan, type of packaging and analytical test procedures shall be similar to those under real time stability studies. (See below). 3. Accelerated stability data results shall enable proposition of a tentative shelf life of 24 months, which shall later be confirmed by completed real time stability studies. 4. The requirement of orientation of containers and container closure systems is equally applicable here as is the case for real time stability studies.
8.2. Real time stability studies Describe briefly the real time stability studies performed to establish the shelf life and storage conditions of the product	1. Real time stability studies should be conducted under controlled conditions in stability chambers and not on open shelves. 2. They should be carried out under zone IV of the world climatic conditions (hot/humid), which are fixed at 30±2°C/65%±5%RH except as may otherwise be recommended for those drugs which require special storage conditions. 3. Sampling should be done at initial, 3, 6, 9, 12, 18, 24, 36 etc. months to establish the stability characteristics of the drug product. 4. Samples from three different

	batches, which are randomly selected to represent the whole batch, should be used for the study. 5. Attributes (parameters) to be tested should be those susceptible to change and are likely to influence the quality, safety and efficacy of the pharmaceutical product. These parameters should at least cover: a) Appearance for all dosage forms b) Assay (stability indicating) for all dosage forms c) Degradation products/ impurities for all dosage forms d) Physicochemical properties such as disintegration, hardness, particulate matter, etc. for all solid dosage forms e) Dissolution for all solid and semi solid oral dosage forms. f) Microbial limits for all dosage forms g) Sterility for parenterals. h) pH for parenterals and liquid preparations. 6. A description of the sampling plan used to select the samples from the test batch for storage and subsequent testing should be given. 7. For liquids, dispersed systems and semi-solid products, samples should be stored in upright, horizontal and inverted positions to ensure full interaction with all primary packaging materials.
8.3 Provide results of stability studies for the three batches tested.	1. Results should be presented in tabular form or graphs (wherever

	possible). 2. Acceptance criteria should be fixed for each test included in the stability study. The criteria can be in the form of numerical limits if results are quantitative (e.g. assay degradation products, particle size, and viscosity). For qualitative tests, the criteria can be pass or fail (e.g. odor, color, appearance). 3. Analytical test procedures shall be fully validated and assays shall be stability indicating. For products with official monographs, the procedures in the current edition of the official compendia stipulated in these guidelines will apply.

9. Labeling requirements

Every immediate container of any product shall be affixed with a label bearing the following particulars pertaining to the contents of such container in clearly legible and indelible letters in either English and/or Kiswahili or both languages. However, for general sales products, labeling in Kiswahili is mandatory.

(a) Proprietary/trade name

(b) The dosage form of the product

(c) Quantitative list of active ingredient(s) in the container expressed in the appropriate unit or volume of the pharmaceutical product.

(d) Name and address of registrant

(e) In case of contract manufacturing, the name and address of manufacturer printed in the same letter size as those of the registrant as follows: *"Manufactured for..... (name and address of registrant) by..... (name and address of manufacturer)"*.

(f) Distribution category

(g) Where applicable the instruction:
"Shake well before use"
"For external use only"

(h) The instruction "keep out of reach of children"

(i) Where practicable, indications and recommended dosage of the pharmaceutical product.

(j) In case of products for injection, route of administration by suitable words or abbreviations such as im, iv, etc.

(k) The batch or lot number of the product

(l) The manufacturing and expiry date of the product

(m) Tanzania registration number

(n) The name and concentration (content) of preservatives, where present

(o) Storage instructions and shelf life

In case the product's package bears both the immediate container label and outer container label, the above requirements shall apply to the outer label as well.

10. Requirements for package inserts

Each package of a product shall be accompanied by a package insert either as a separate entity or as an integral part of the package on which the following information is printed in legible letters either in English or Kiswahili or both under the headings specified below:

(a) Name and dosage form of the product

(b) Identification (description of the product and package)

(c) Quantitative list of active ingredients in a dosage unit or suitable mass or volume or unit of the product

(d) Indications

(e) Dosage regimen and directions for use

(f) Contraindications

(g) Side effects and adverse reactions

(h) Drug interactions

(i) Precautions and warnings

(j) Symptoms and treatment of overdose.

(k) Presentation (packing and pack size)

(l) Storage instructions and shelf life

(m) Name and address of manufacturer and country of origin

(n) Date of publication of the insert

11. An independent expert report critically examining the data on quality and making considered opinion supported with references from peer review literature.

CHAPTER V

SAFETY DATA

The requirement for submission of safety data is applicable for products which are **not official** in current editions of pharmacopoeia and for herbal drugs which are **not listed** in the current WHO Monographs on Selected Medicinal Plants.

1. Provide full information to support safety of the herbal drug by submitting results of the following tests:

   (i) Acute toxicity tests using at least two species one of them being a non rodent.

   (ii) Subacute toxicity tests

   (iii) Chronic toxicity tests

   (iv) Mutagenicity tests using salmonella (Ames test) or other tests

   (v) Teratogenicity tests if a product is to be administered to pregnant women

   (vi) Immuno toxicity (tests for allergic reactions)

   (vii) Carcinogenicity tests

   (viii) Reproductive toxicity tests

2. For each of the above tests applicants will be required to provide protocol or study plan and amendments bearing signatures of study director and quality assurance person.

   The protocol shall include:

   (i) Name of study director, principal investigators, their qualifications and full addresses.

   (ii) Details of all test items including transportation, storage, formulation data and quality control data.

   (iii) Information on test system (supplier, animal husbandry, species, justification for use, strain).

(iv) Curriculum vitae (CV) of all personnel involved in the study.

(v) Copies of standard operating procedures and revisions if any for each of the tests.

(vi) Copies of all raw data including manuscripts and printouts.

(vii) Copy of final report on safety of the product signed by the study director and quality assurance person.

3. An independent expert report critically examining data and making considered opinions supported with references from peer review literature.

CHAPTER VI

EFFICACY DATA

The requirement for submission of efficacy data is applicable for products which are not official in current editions of pharmacopoeia and for herbal drugs which are not listed in the current WHO Monographs on Selected Medicinal Plants. It shall be noted that only those therapeutic uses which are established through clinical studies are acceptable for herbal drugs listed in the current WHO Monographs on Selected Medicinal Plants. The rest of the herbal drugs shall be required to provide evidence of efficacy as outlined below.

1. Provide evidence of efficacy of the herbal drug by submitting clinical trial reports for phases I, II and III. Evidence should be provided to ensure that phases II and III trials are properly controlled and randomized using either a placebo or active drug as the case may be. The reports shall at least include study design, names, qualifications and addresses of investigators, study site, study dates, details of preparations used, standard operating procedures and revision if any, copies of raw data, characterization of study subjects, inclusion and exclusion criteria, results, discussion and conclusions.

2. Copy of the final report on efficacy of the product which is signed and dated by the study director and quality assurance person.

3. Provide copy of ethical clearance.

4. An independent expert report critically examining data and making considered opinions supported with references from peer review literature.

APPENDIX

TFDA NO.....

THE UNITED REPUBLIC OF TANZANIA
MINISTRY OF HEALTH

TANZANIA FOOD AND DRUGS AUTHORITY

APPLICATION FORM FOR REGISTRATION OF HERBAL DRUG

Date:..... Application Number .....for official use only)

1.0 Particulars of products

1.1 Product Name: .....

1.2 Pharmaceutical dosage form:.....
.....

1.3 Therapeutic use(s):.....
.....

1.4 Distribution category:.....

1.5 Type of container:
.....
.....
.....

1.6 Pack size(s):.....
.....

1.7 Shelf life.....:.....
.....

1.8 Shelf life after first opening of container (where applicable).....

……

1.9 Shelf life after reconstitution (where applicable)……

……

1.10 Storage conditions:……

……

2.0 Particulars of applicant

Name:……

Physical Address: ……

……

Postal Address:……

Country: ……

Phone:……

Fax:……

E-mail……

3.0 Particulars of a responsible person (for herbal drugs to be imported only)

Name:……

Physical address:……

……

Postal address:……

……

Phone:……Fax:……E-mail……

4.0 Manufacturer and qualified person for manufacture of the herbal drugs

(a) Manufacturer

Name:……

Physical address:……

……

Postal address:……

……

Phone:……..Fax:……..E-mail……

(b) Qualified person:

Name:……

……

Qualifications:……

……

Address:……

……

Phone:……..Fax:……..E-mail……

5. Status of registration of the product in the country of origin, authorization/registration number and date. State whether it is registered in any of the following countries: ICH/VICH countries, Australia, Canada, South Africa, Egypt, Malaysia and Zimbabwe.

……

……

6. Product composition

6.1 Active ingredient(s)

SN	Name	Specification (BP, USP, etc)	Quantity used per dosage unit	Reason for inclusion

6.2 Excipients

SN	Name	Specification (BP, USP, etc)	Quantity used per dosage unit	Reason for inclusion

7. Declaration by an applicant

I, the undersigned certify that all the information in this form and accompanying documentation is correct. I further confirm that the information referred to in my application file is available for verification during GMP inspection.

I also agree that I am obliged to follow the requirements of the Tanzania Food, Drugs and Cosmetics Act 2003 which are related to herbal drugs.

Name: ……

Position in the company:……

Signature: ……

Date:…… Official stamp:……