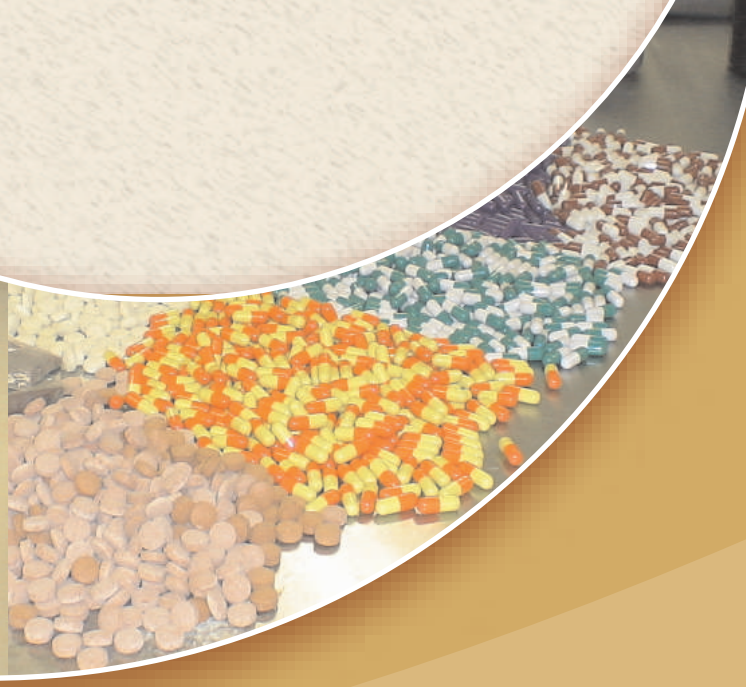
GUIDELINES FOR REGISTRATION OF TRADITIONAL MEDICINES IN THE WHO AFRICAN REGION



World Health Organization
Regional Office for Africa

AFR/TRM/04.1

GUIDELINES FOR REGISTRATION OF TRADITIONAL MEDICINES IN THE WHO AFRICAN REGION

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AFRO Library Cataloguing-in-Publication Data

Title : Guidelines for registration of traditional medicines in the WHO African Region

1. Medicine, African Traditional
2. Credentialing - methods
3. Guidelines
4. Africa

ISBN : 978 929 023 1479 NLM Classification: WB 55.A3)

Printed in India
First printed, 2004

Contents

Foreword

Traditional medicines have been used by humankind for the treatment of various diseases since long before the advent of orthodox medicine, and to this day, serve the health care needs of the majority of the population living in the WHO African Region. The criteria for evaluating traditional medicines, like those for conventional medicines, are quality (i.e. medicines should be well formulated and possess consistent quality from batch to batch as specified in the official pharmacopoeia chosen as a standard), safety (i.e. medicines should not present risks that are disproportionate to their benefits) and efficacy (i.e. medicines should be effective for the indications claimed and should be clinically significant and useful). However, most traditional medicines that are in use today, many of which are sold to the public via outlets such as open markets, stops and homes, lack scientific evidence of their quality, safety and efficacy. Moreover, the development of regulatory systems for traditional medicines varies widely between countries of the WHO African Region. Less than one third of the countries in the WHO African Region have any form of regulation on traditional medicines. Most countries have yet to establish safety monitoring and pharmacovigilance systems for pharmaceuticals, let alone for herbal medicinal products currently on the market. This scenario poses a unique set of challenges for health care services in the WHO African Region.

Recognizing the importance of the role of traditional medicines in the WHO African Region and the potential for adverse health consequences through their misuse, the Fiftieth Session of the WHO Regional Committee for Africa adopted — in Ouagadougou, Burkina Faso on 31 August 2000 — its Regional Strategy on Promoting the role of Traditional Medicine in health systems: a strategy for the African Region by its Resolution AFR/RC50/R3. That resolution requested the WHO Regional Director, among others, to develop guidelines for the formulation and evaluation of national policies on traditional medicine, to advise countries regarding relevant legislation and documentation of medicines, and to urge Member States to produce evidence on the quality, safety and efficacy of traditional medicines.

In order to assist Member States in establishing mechanisms for evaluating traditional medicines for registration purposes, the WHO Regional Office for Africa, in collaboration with the Department of Essential Drugs and Medicines Policy, WHO, organized a series of regional workshops on the regulation of traditional medicines. The first regional workshop, which was held in Johannesburg, South Africa, from 1 to 3 April 2003, reviewed and adopted the present set of guidelines on the registration of traditional medicines. The guidelines were subsequently used to train representatives of national drug regulatory authorities from a number of countries within the WHO African Region at a follow-up workshop, held in Madrid, Spain, from 13 to 14 February 2004.

These guidelines have been expressly developed in order to facilitate the registration, marketing and distribution of traditional medicines of assured quality in the WHO African Region. This document is particularly relevant to those countries that have already put in place mechanisms for the registration of traditional medicines. I call your attention to the section of the guidelines that is devoted to the classification of traditional medicines (which can range from the traditional health practitioner's remedies to the traditional medicine derived from scientific research) according to the mode of preparation, the indication and the extent of development of the remedy. Use of this classification system should assist the work of national drug regulatory authorities when undertaking the assessment of the documentation submitted with the applications for registration of herbal medicines. The guidelines also set out proposals regarding the minimum regulatory requirements for the registration of each category of traditional medicine in terms of the quality of raw plant materials as well as the quality, safety and efficacy of the finished product which will be useful guidance not only to the national drug regulatory authorities, but also to industries and research institutions involved in the development of traditional medicines. Issues related to labelling and advertisement requirements, registration procedures, production authorization and distribution channels, and the organization of pharmacovigilance are also covered.

It is my hope that Member States using these guidelines will send their comments to WHO so that subsequent revisions to the document can be based on their experiences.

I am very grateful to the Canadian International Development Agency for providing funds for this publication and also to the Department of Essential Drugs and Medicines Policy, WHO, for its support in the publication of the present guidelines.

Dr Luis Gomes Sambo
Regional Director

Acknowledgements

The WHO Regional Office for Africa is indebted to all participants in the First Meeting of the WHO Regional Expert Committee on Traditional Medicine, which was held in Harare, Zimbabwe, from 19 to 23 November 2001 and the Regional Meeting on Integration of Traditional Medicine into Health Systems: Strengthening Collaboration Between Traditional and Conventional Health Practitioners, which was held in Harare, Zimbabwe, from 26 to 29 November 2001, who provided valuable comments on earlier versions of this document.

The WHO Regional Office for Africa is also greatly indebted to the national health officials from national drug regulatory authorities and representatives of other national health authorities who contributed much to the success of First Regional Workshop on Regulation of Traditional Medicines held in Johannesburg, South Africa (1–3 April 2003), at which the draft guidelines were reviewed and adopted. The Second Regional Workshop on Regulation of Traditional Medicines (Madrid, Spain, 13–14 February 2004), which was also organized by the WHO Regional Office for Africa in collaboration with Department of Essential Medicines and Drug Policy, WHO, was held in order to promote the use of the guidelines to support the registration of safe, effective traditional medicines throughout the WHO African Region. The valuable contribution of all participants in achieving this objective is also gratefully acknowledged.

Special thanks are due to Dr Rufaro Chatora, former Director, Division of Health Systems and Services Development, WHO Regional Office for Africa, for his expert guidance throughout the preparation of this document.

Dr Jean-Marie Trapsida, Coordinator, Essential Drugs and Medicines Policy, WHO Regional Office for Africa, is acknowledged for his guidance and contribution during the preparation of these guidelines. The valuable comments were received from Dr Xiaorui Zhang, Coordinator of Traditional Medicine Programme, Department of Essential Drugs and Medicines Policy, WHO.

Appreciation is also extended to the staff of the Department of Essential Drugs and Medicines Policy, WHO, particularly those involved in the Traditional Medicine Programme and the Drug Action Programme for their assistance in organizing the First and Second Regional Workshops on Regulation of Traditional Medicines held in Johannesburg, South Africa, in April 2003 and in Madrid, Spain, in February 2004, respectively. In the case of the latter, the additional

support provided by the Spanish Agency for Medicines and Healthcare Products, Madrid, Spain, is also gratefully acknowledged.

The WHO Regional Office for Africa is especially grateful to the Canadian International Development Agency for providing financial support for the two regional workshops mentioned above.

The WHO Regional Office for Africa is very much indebted to the Government of Luxembourg for providing funding via the Traditional Medicine Programme, Department of Essential Drugs and Medicines Policy, WHO, for the First Regional Workshop on Regulation of Traditional Medicines, Johannesburg, South Africa, 1–3 April 2003, and also for printing and publishing these guidelines.

Last, but not least, we thank Dr Jean-Baptiste Nikiéma, Member, WHO Regional Expert Committee on Traditional Medicine, (Ouagadougou, Burkina Faso), Dr Marianne Ngoulla, Division of Health Systems and Services Development, WHO Regional Office for Africa (2000-2001), Dr Charles Wambebe, Traditional Medicine Programme (2002-2004), Division of Health Systems and Services Development, WHO Regional Office for Africa and Dr Ossy MJ Kasilo, Regional Adviser, Traditional Medicine Programme, Division of Health Systems and Services Development, WHO Regional Office for Africa, for the time they have devoted to the development and finalization of this document.

Abbreviations

ADB	African Development Bank
AFDRAN	African Drug Regulatory Authorities Network
ARIPO	The African Regional Industrial Property Organization
ECOWAS	Economic Community of West African States
FAO	Food and Agriculture Organization of the United Nations
HIV/AIDS	Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome
IUCN	International Union for the Conservation of Nature
NDRAs	National drug regulatory authorities
OAPI	African Organization for Intellectual Property
OAU	Organization of African Unity
SADC	South African Development Community
TB	Tuberculosis
THPs	Traditional health practitioners
UMEOA	Monetary and Economic Union of West Africa
UNIDO	United Nations Industrial Development Organization
WHO	World Health Organization
WIPO	World Intellectual Property Organization

Introduction

The role of traditional medicines in primary health care

Many countries in the WHO African Region are encountering problems in providing their people with equitable access to health care; at present, only about one half of the population in the Region has access to conventional health care. Such considerations aside, traditional medicines continue to be popular for both historical and cultural reasons. It has been estimated that around 80% of the population living in the WHO African Region rely on traditional forms of medicine to meet their health care needs *(1)*. In countries for which more detailed data are available, the percentage of the population that uses traditional medicine ranges from 90% in Burundi and Ethiopia, to 80% in Burkina Faso, the Democratic Republic of Congo and South Africa; 70% in Benin, Cote d'Ivoire, Ghana, Mali, Rwanda and Sudan; and 60% in Tanzania and Uganda *(1)*. According to a survey conducted by WHO Roll Back Malaria, in Ghana, Mali, Nigeria and Zambia, 60% of febrile cases among children, presumably due to malaria, were treated with herbal medicines at home in 1998 *(2)*. A recent study published by UNAIDS *(3)*, suggests that about two thirds of AIDS patients in developing countries use traditional medicines to obtain symptomatic relief and manage opportunistic infections.

The importance of traditional medicine in primary health care was clearly emphasized in the Alma-Ata Declaration of 1978 and also in several WHO governing body recommendations which address the strategic options that are expected to help achieve health for all *(4-7)* Partner agencies of the United Nations, such as the Food and Agriculture Organization of the United Nations (FAO), the International Union for the Conservation of Nature (IUCN), the United Nations Industrial Development Organization (UNIDO) and the World Intellectual Property Organization (WIPO), and other African and international organizations, including African Development Bank (ADB), the Organization of African Unity (OAU), the African Regional Industrial Property Organization (ARIPO) and the African Organization for Intellectual Property (OAPI) and the World Bank, have also stressed the importance of traditional medicine.

These policy orientations notwithstanding, the reality is that few countries have developed national policies, legal frameworks, and codes of ethics and conduct for the practice of traditional medicine. Some countries have set up associations of traditional health practitioners (THPs), established management bodies responsible for coordinating traditional medicine activities and/or developed programmes for the training and continuing education of THPs, including traditional birth attendants. A number of research institutions, including several WHO collaborating centres, are currently carrying out research on traditional medicines. Furthermore, some countries in the WHO African Region have embarked upon the local production, albeit on a pilot-scale, of various herbal preparations for the treatment of common ailments and priority diseases such as malaria, human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS), sickle-cell anaemia, hypertension and diabetes. Some of these herbal medicines have been registered and included in national essential medicine lists. However, most countries in the Region have not put in place mechanisms for registering traditional medicines and much needs to be done in terms of the formalization of traditional medicines with respect to their safety, efficacy and quality.

It is against this background that the Traditional Medicine Programme of the WHO Regional Office for Africa has developed these guidelines for registration of traditional medicines. It is hoped that these guidelines will go a long way to increasing access to safe, effective traditional medicines in health care systems as a viable supplement to conventional medicines, and thereby accelerate progress towards achieving health for all in the Region.

Purpose and target audience of the guidelines

The purpose of this document is to propose to Member States a framework for facilitating the registration of traditional medicines. The proposed framework, which has a regional perspective, is intended to accelerate the registration and circulation of standard African traditional medicines within the WHO African Region, on the basis of criteria of pharmaceutical quality, safety of use and therapeutic efficacy.

The guidelines are aimed at national drug regulatory authorities (NDRAs), manufacturers, traditional health practitioners and institutions engaged in drug research and development, who

should ensure that their products satisfy the requirements laid down in this document. The guidelines can also be used for training and teaching purposes, in particular, for teaching undergraduate and postgraduate pharmacy, and for training pharmacy technicians, nurses and medical students, related health professions and agencies involved in the development of traditional medicine in the WHO African Region.

Structure of the document

The document is divided into three parts. Part I outlines the history of the development of the guidelines, the guideline objectives, and a classification system for traditional medicines Part II lays down proposals for the minimum regulatory requirements for the registration of each category of traditional medicine, in terms of the quality of plant raw materials as well as quality, safety and efficacy of the finished product and labelling and packaging. Part III proposes procedures for the registration of traditional medicines and addresses a range of issues related to the registration of traditional medicines, marketing and advertising; post-market surveillance and the organization of pharmacovigilance; and production authorization and distribution channels. A list of further reading, which includes a number of information sources that were used to support the preparation of the guidelines, is also provided.

Feedback

Comments and observations on these guidelines from users would be most welcome and should be sent to the following address:

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Part - I

1. Background to the development of the guidelines

The term "traditional medicine" refers to the use of indigenous medicinal and aromatic plants, animal parts, or organic and inorganic materials for preventive and therapeutic purposes. Traditional medicines are medicinal products that contain as active ingredients aerial or underground parts of plants, or other plant materials, or combinations thereof, whether in the crude state or as plant preparations. *(8)* In this document, the terms "traditional medicines" and "herbal medicines" are used interchangeably.

Traditional medicine represents an important component part of health care provision in many African countries. In some countries, it has been estimated that up to 90% of the population rely on traditional medicines for their health care needs. Currently, traditional medicines are used to treat a wide range of illnesses, including diabetes, diarrhoea, HIV/AIDS, hypertension, microbial infections and sickle-cell anaemia throughout the WHO African Region.

The use of herbal medicines in the WHO African Region is largely based on oral tradition within the family or community. These herbal products are sold to the public in open markets and shops, and from traditional health practitioners' homes. However, most traditional medicines, which are claimed to provide "effective cures" for various diseases, lack scientific evidence of their safety, efficacy or quality.

The regulation of traditional medicine varies widely in the different countries in the WHO African Region. The results of an unpublished survey conducted by WHO in 1998 indicate that of the 36 participating countries, only 12 had formulated national policies on traditional medicine and only eight had regulations on traditional medicines. Generally speaking, researchers in the WHO African Region lack the facilities for the assessment of the quality, safety and efficacy of traditional medicines, partly because of the complex composition of many traditional medicines.

Faced with these realities, the Forty-ninth Session of the WHO Regional Committee for Africa, held in Namibia in 1999, invited the WHO Regional Office for Africa to develop a

comprehensive regional strategy on traditional medicine. Through resolution AFR/RC49/R5[2], the WHO Regional Committee for Africa requested that the WHO Regional Director, among others, support Member States in carrying out research on medicinal plants and promoting their use in the health care delivery system. In response to these recommendations, the WHO Regional Office for Africa developed a strategy paper entitled, *Promoting the role of traditional medicine in health systems: a strategy for the African Region,* which was subsequently adopted by the Fiftieth Session of the WHO Regional Committee for Africa, held in Ouagadougou, Burkina Faso, in 2000. Specifically, Resolution AFR/RC50/R3[1] requested the WHO Regional Director, among other things, to support Member States in the development of guidelines for the formulation and evaluation of national policies on traditional medicine and to advise countries regarding the relevant legislation for the practice of traditional medicine. It was envisaged that this could be achieved through the institutionalization of traditional medicines.

Although traditional medicines have been used for many centuries, they remain largely unregulated. According *to* the *Health-for-All Policy for the 21st Century in the African Region: Agenda 2020 (9),* the non-regulation of traditional medicine has created a complex situation which poses new challenges. In particular, it was emphasized that the promotion of the role of traditional medicine in health systems requires the provision of medicines that have valid data regarding their safety, pharmaceutical qualities and therapeutic efficacy. To this end, Member States should be assisted to put in place a regulatory framework for accelerating the registration of traditional medicines as a matter of urgency.

The present set of guidelines, which include a classification system for traditional medicines and a list of the minimum requirements on quality, safety and efficacy for their registration, have been developed in response to the need for a regulatory framework for traditional medicines. Draft versions of the guidelines were reviewed and revised during a series of expert meetings, namely the First Meeting of the WHO Regional Expert Committee on Traditional Medicine (held in Harare, Zimbabwe, 19-23 November 2001), the Regional Meeting on Integration of Traditional Medicine into Health Systems: Strengthening Collaboration Between Traditional and Conventional Health Practitioners (held in Harare, Zimbabwe, 26-29 November 2001) and at the Second Meeting of the WHO Regional Expert Committee on Traditional Medicine (held in Libreville, Gabon, 4–8 November 2002).

[1] *Promoting the role of traditional medicine in health systems: a strategy for African countries with region*. Harare, World Health Organization Regional Office for Africa, 2001, Resolution, (AFR/RC50/R3).

[2] Essential Drugs in the WHO African Region: Situation and Trend Analysis (Resolution, AFR/RC49/R5), World Health Organization Regional Office for Africa, Harare, 2000.

The final amendments were made at the First Regional Workshop on Regulation of Traditional Medicines, held in Johannesburg, South Africa, from 1 to 3 April 2003, and the resulting document, *GUIDELINES FOR REGISTRATION OF TRADITIONAL MEDICINES IN THE WHO AFRICAN REGION*, formally adopted. The meeting, jointly organized by the WHO Regional Office for Africa and the Department of Essential Medicines and Drug Policy, WHO, was attended by representatives of 19 national drug regulatory authorities and experts from 17 countries: Benin, Burkina Faso, Democratic Republic of Congo, Côte d'Ivoire, Ghana, Ethiopia, Kenya, Madagascar, Mali, Mozambique, Nigeria, South Africa, Swaziland, Tanzania, Uganda, Zambia and Zimbabwe.

The Second Regional Workshop on Regulation of Traditional Medicines was held in Madrid, Spain, from 13-14 February 2004. The purpose of this follow-up workshop was to promote the registration and marketing of safe, effective and good quality traditional medicines within the WHO African Region by providing training in the application of the guidelines to national drug regulatory authorities. In so doing, the workshop formed an important part of WHO's overall effort to support capacity building for the regulation of herbal medicines in countries of the WHO African Region according to their national situation. The workshop brought together 15 of the 19 invited NDRAs and experts from Angola, Burkina Faso, Cameroon, Congo, Ghana, Lesotho, Liberia, Madagascar, Namibia, Niger, Nigeria, Senegal, Sierra Leone, Togo and Zimbabwe[3]. The workshop was coorganized by the WHO Regional Office for Africa and the Department of Essential Drugs and Medicines Policy, WHO, with support from the Spanish Medicines Agency and Healthcare Products, Madrid, Spain and the Canadian International Development Agency, in Montreal, Quebec. The workshop was scheduled to coincide with the International Conference of Drug Regulatory Authorities (Madrid, Spain, 16–19 February 2004) so as to provide an opportunity for delegates to participate in both events.

Purpose and objectives of the guidelines

The purpose of this document is to propose to Member States a framework for facilitating the registration of traditional medicines. The proposed framework, which has a regional perspective and is based on the criteria of pharmaceutical quality, safety of use and therapeutic efficacy, should accelerate the registration and circulation of standardized African traditional medicines within the WHO African Region.

[3] The Democratic Republic of Congo, Gambia, Mauritius and Rwanda were invited but were unable to attend.

General objectives

The overall objective of the guidelines is to facilitate the registration, marketing and distribution of traditional medicines of consistent quality in the WHO African Region.

Specific objectives

The specific objectives of the guidelines are as follows:

- to propose a classification scheme for traditional medicines;
- to propose general minimum regulatory requirements for the registration of traditional medicines;
- to formulate proposals for facilitating the introduction of safe and effective traditional medicines of consistent quality into the African market.

Definition and classification of traditional medicines

Definition of traditional medicines

For the purpose of this document, the term "traditional medicine" is taken to mean any finished, labelled medicinal product that contains as its active ingredient(s) aerial or underground parts of plants, or other plant materials, or combinations thereof, whether in the crude state or as plant preparations. Plant material includes juices, gums, fatty oils, essential oils and any other substances of this nature. Traditional medicines may contain conventional excipients in addition to the plant-based active ingredients. In some cases, they may also contain, by tradition, natural organic or inorganic ingredients which are not of plant origin. However, products to which chemically-defined active substances have been added, including for example, synthetic compounds and/or isolated constituents from herbal materials, are not considered to be traditional medicinal products.

Classification of traditional medicines

A large variety of different types of traditional medicines are available on the African market, ranging from raw plant materials, through processed, packaged remedies, to imported herbal products. It would be very difficult, if not impossible, to implement a mechanism for the registration of traditional medicines in the WHO African Region without the use of an appropriate classification system for products of this nature.

Four categories of traditional medicines, based on their mode of preparation, the indication, and extent of the development of the traditional medicine relative to the traditional remedy used, are thus distinguished as set out below.

Category 1

Category 1 traditional medicines are medicines that have been prepared by traditional health practitioners for treatment of individual patients; they have the following characteristics:

- Prepared in an extemporaneous manner and according to traditional methods;
- Safety and efficacy are justified by a long period of use;
- Category 1 medicines are not directly controlled by national drug regulatory agencies but traditional health practitioners who supply them should be certified by the registration of their practice;
- If, however, a category 1 medicine is introduced into the market, it must meet the minimum regulatory requirements for the registration of traditional medicines.

Category 2

A category 2 traditional medicine is one that is widely used in the community but has a commercial possibility. It is characterized as follows:

- Traditionally used in a given locality and very well known by the local population, both in terms of composition and treatment;
- The formulation is well known and its preparation is according to traditional methods;
- Safety and efficacy are justified by a long period of use;
- It is available to local people free of charge;
- However, if a category 2 medicine were to go on the market, it would have to meet the general minimum requirements for the registration of traditional medicines.

Category 3

A category 3 traditional medicine is one that has been developed through scientific research. It has the following characteristics:

- It has been developed by research based on ethno-medical use;
- The formulation, dosage, dosage form and therapeutic use are based on research data;
- It is produced on a semi-industrial or industrial scale;
- Safety and efficacy are based on research data derived from standard scientific and clinical investigations;
- Category 3 traditional medicines may be used within a research establishment;
- If, however, a category 3 medicine goes on to the market, it must meet the general minimum requirements for the registration of traditional medicines.

Category 4

Category 4 traditional medicines are imported traditional medicines, and as such are distinguished by the following:

- It originates from a foreign country, either within or outside the WHO African Region;
- It should meet the definition of traditional medicines;
- It should be registered in the originating country;
- It should meet the requirements for the regulation of traditional medicines of the country into which it is being imported.

Part - II

The minimum regulatory requirements for the registration of traditional medicines: safety and efficacy

General minimum requirements

Safety

(a) Botanical identification/authentication

Latin name (genus and species) of the plant species, local names and family.

(b) Biological information (via literature search/database)

- Biomedical medical information regarding the safety and efficacy of the product.
- In the absence of published results of toxicological studies, documented experience of long-term use should form the basis of the risk assessment. However, even in cases of traditional medicines used over a long period, chronic toxicological risk may have occurred but may not have been recognized.
- Identification of toxic plants from national pharmacopoeia *(10)* or international documents, such as the *African Pharmacopoeia (11-12)* or relevant WHO monographs *(13)* and other well-established biomedical documentation.

(c) Toxicity studies

- If the product has a long history of use without demonstrated harm, specific restrictive regulatory action is not necessary, unless new evidence indicates a need for a revised risk–benefit assessment.

- If there is a known toxicological risk, standard toxicological studies are mandatory. Data derived from such studies should be appropriately documented and submitted to the regulatory authorities. Toxicity data should be submitted if long-term traditional use *cannot be* documented or if there are doubts about safety.

- The absence of any reported or documented side-effects is not an absolute assurance of safety for traditional medicines; some toxicological tests may therefore be

necessary. Suggested tests should include those for immunotoxicity (e.g. tests for allergic reactions), genotoxicity, carcinogenicity and reproductive toxicity through long-term use.

(d) Posology
(e) Dosage forms
(f) Adverse reactions
(g) Contraindications
(h) Warnings
(i) Precautions

Efficacy

Therapeutic activity refers to the successful prevention, diagnosis and treatment of physical and mental illness; the improvement in the symptoms of illness; as well as the beneficial alteration or regulation of the physical and mental status of the body. The active ingredients of a traditional medicine are those that have therapeutic activity.

(a) *Assessment of efficacy*

- In the case of traditional medicines, the requirements for proof of efficacy will depend on the kind of indications for use and individual experiences as recorded in reports from physicians, traditional practitioners or treated patients;

- If use of a traditional medicine has not been documented, or in cases where a new medicine consists of traditionally-used plants for a new indication, appropriate clinical evidence of efficacy is required.

(b) Active ingredients

- The preparation of medicines whose active ingredients have been identified should be standardized so that each batch contains a defined amount of the active ingredients, assuming adequate analytical methods are available;

- In cases where it is not possible to identify the active ingredients, the whole traditional medicine may be considered as one active ingredient.

(c) Evaluation of efficacy

- For uses supported by clinical data (i.e. including medical indications which are well-established in some countries and which have been validated by clinical trials, the results of which are recorded in the scientific literature);

- For uses described in pharmacopoeias and other well-recognized documents (i.e. medicinal uses that have been well-established in many countries and are included in official pharmacopoeias or official government monographs);

- For uses described in traditional medicine (i.e. indications described in non-official pharmacopoeias and other forms of literature or purely traditional uses).

(d) Guidelines for clinical evaluation of traditional medicines

The WHO Regional Office for Africa has developed guidelines for clinical study of traditional medicines in the WHO African Region *(14).* Is a generic document regarding clinical evaluation of traditional medicines which also contains peculiarities pertaining to the clinical studies of traditional medicines against HIV/AIDS, malaria, sickle-cell anaemia, diabetes and hypertension.

Specific requirements

Member States are expected to develop specific regulatory requirements regarding the safety and efficacy of each category of traditional medicines based on the general minimum regulatory requirements outlined in section 4.1 above and other national specifications.

Minimum regulatory requirements for the registration of traditional medicines: quality control

General minimum requirements

Raw materials

(a) Identification of plant(s)

- Definition (i.e. Latin name of the plant including Genus, species, varieties family);
- Synonyms (i.e. legitimate Latin binomial synonyms for the plant);
- Selected vernacular names (i.e. a selective list of vernacular names for the plant);
- Geographical distribution (i.e. the natural distribution in the country or region, and/or whether the plant(s) is cultivated or imported);
- Description (i.e. a brief description of the living plant including photographs and/or drawings).

(b) Part of the plant used and the condition of the plant material used

- General appearance.
- Organoleptic properties.
- Microscopic characteristics.
- Powdered plant material.

(c) General identity tests

- Chemical, biological or physical assays.

(d) Purity tests

- Microbiological and chemical.
- Foreign organic matter.
- Total ash, acid-insoluble ash and sulfated ash.
- Water-soluble extractive.
- Alcohol-soluble extractive.
- Loss on drying.
- Swelling index.
- Pesticide residues.
- Heavy metals.
- Radioactive residues.
- Other purity tests.

Finished products

(a) Qualitative and quantitative composition of the active components;

(b) Quantity and type of excipients;

(c) Quantification of the active ingredient;

(d) Description of the process of manufacture;

(e) Specifications of quality of the finished product;

(f) Methods of analysis;

(g) Stability studies;

(h) Certificate of registration in the country of origin, preferably according to national regulatory requirements;

(i) Good manufacturing practices in accordance with the official national standards;

(j) Packaging;

Specific Requirements

Member States are expected to develop specific regulatory requirements regarding the quality control of each category of traditional medicines based on the general minimum requirements outlined in section 5.1 and other national specifications.

Minimum regulatory requirements for traditional medicines: labelling and packaging

Labelling

Labels should provide the following information:

- The name of product.
- A quantitative list of the active ingredients, including the plant names (if the product is from abroad, the Latin name should be given).
- Dosage form.
- Therapeutic indications.

- The minimum, average and maximum dosage should be clearly stated and, if appropriate, specified for children and the elderly, as well as information about:
  - the mode of administration;
  - the duration of use;
  - major adverse effects, if any;
  - over-dosage information;
  - contraindications, warnings, precautions and major drug interactions, if possible;
  - manufacturing date.
- Expiry date.
- Lot number.
- Name of manufacturer or company with full address.

Packaging

Packaging specifications should be in accordance with national regulatory requirements.

Part - III

Regulation of the advertising of traditional medicines

The national authority responsible for the regulation of traditional medicines should also vet advertisements prior to their release to ensure that the public receives correct information about the product devoid of ambiguous or bogus claims.

The regulatory authority should issue advertising permits only after the satisfactory evaluation of the content of any advertisement. The print and electronic media should be notified to ensure that every advertiser of traditional medicine products obtains the "ADVERT PERMIT" from the national regulatory authority before an advertisement can be circulated.

Post-market surveillance

Currently, genuine information about the adverse effects of, and/or adverse drug reactions to, herbal medicines is often masked or overshadowed by anecdotal evidence of adverse events that are more than likely attributable to either poor product quality or improper use of herbal products.

Depending on the situation of traditional medicine in a particular country, governments may need to establish national surveillance systems at different levels of the health sector in order to monitor and evaluate any reported adverse effects of traditional medicine. Knowledgeable researchers and practitioners of traditional medicine should be consulted during the development of such systems.

The evaluation of adverse effects should be based on appropriate methods of determining causality. Such methods include the use of suitable survey instruments (e.g. questionnaires) to determine adverse events experienced by target groups (i.e. patients, practitioners); prospective and retrospective studies to determine adverse effects in specific settings; and post-market surveillance of new devices (both herbal medicines and equipment used in traditional procedure-based therapy) in which a comprehensive evaluation of any adverse effect is documented.

In order to enhance the safety of patients and consumers using traditional medicines, existing national safety monitoring and pharmacovigilance systems should be expanded in scope to include herbal medicines. If such systems do not already exist, they should be established as a matter of priority and provision made for traditional medicine at the outset.

WHO has produced a series of guidelines for safety monitoring, including *Safety monitoring of medicinal products: guidelines for setting up and running of a pharmacovigilance centre (15) and WHO guidelines on safety monitoring and pharmacovigilance of herbal medicines (16)* and countries wishing to set up safety monitoring centres and programmes are encouraged to consult these documents.

Other issues related to the registration of traditional medicines

Ethics

International ethical guidelines for biomedical research involving human subjects should be followed in all clinical trials involving traditional medicines *(17)*.

Ideally, an ethics committee should review the protocol for each clinical trial, according to each institution's guidelines. Whenever applicable, rescue treatment may be provided to patients involved in a clinical trial involving the use of a placebo or unproven treatment. Use of the rescue treatment may be a secondary outcome measure.

In some countries and hospitals, there are ethical issues that restrict the use of clinical trials. In some cases, the use of a placebo is illegal, particularly for patients suffering from certain illnesses, such as cancer. Clinical trials must always be conducted within the framework of the prevailing law in a given country or state.

Proposals for accelerating the marketing of traditional medicine

Traditional medicine plays an important role in the provision of health care in Africa. However, this presupposes an efficient circulation of traditional medicines throughout the continent, with the same guarantees in terms of pharmaceutical quality, safety, and therapeutic efficacy as orthodox/allopathic medicine. The establishment of national expert committees for traditional medicines, according to the guidelines given below and based on country experiences such as Burkina Faso *(18)*, Ghana *(19)*, Madagascar *(20)* and Nigeria *(21)*, should help to accelerate the marketing of these medicines and facilitate their circulation throughout the entire WHO African Region.

National expert committees for the evaluation of traditional medicines

A national expert committee plays an operational role by:

- evaluating applications for a registration licence;
- evaluating applications for authorizations to conduct clinical trials.

The national expert committee also plays a conceptual role by:

- coordinating the development of a national compendium of medicines;
- coordinating the development of an inventory of traditional medicinal plants at national level;
- ensuring the promotion of traditional medicines.

The creation, attribution and functioning of national expert committees should be fixed by decree. The terms of reference, which should be approved by the appropriate national authority, will specify its composition and determine the period for the technical analysis of the applications, which should not exceed three months.

The national expert committee should be composed of experts covering at least the following main areas:

- systematic botany;
- pharmacognosy;
- pharmacology;
- pharmacy;
- toxicology;
- galenics;
- internal medicine;
- haematology;
- sociology/anthropology;
- drug regulation;

Permanent members should be appointed for a period determined by the national competent authority, and which should be renewable for a second term. In addition, the committee may elect expert non-permanent members to serve at each of its meetings; non-permanent members would be appointed by the chair of the committee, according to the kind of expertise required for the applications submitted for evaluation. Preferably, the committee should meet in an ordinary session once every three months.

Subregional expert committees for the evaluation of traditional medicines

With a view to facilitating the circulation of traditional medicines within Member States, it is desirable to encourage regionalization of registrations. In this regard, the creation of subregional expert committees to ensure the technical evaluation of applications is proposed. These committees may be attached to existing subregional organizations, such as the Monetary and Economic Union of West Africa (UMEOA), the Economic Community of West African States (ECOWAS), the Common Market of Eastern and Southern Africa (COMESA) and the Southern African Development Community (SADC).

The primary functions of subregional expert committees are as follows:

- evaluating applications for a licence;
- evaluating applications for authorization to conduct clinical tests.

Additional functions include:

- developing and validating protocols;
- auditing laboratories and research structures for approval;
- evaluating pharmacovigilance data;
- developing subregional compendiums;
- preparing inventories of medicinal plants and traditional medicinal products within the subregion;
- selecting and improving laboratories for ensuring quality control of traditional medicines;
- selecting and improving centres for clinical evaluation of traditional medicines;
- developing pharmacopoeias;
- creating and maintaining a subregional data bank;
- strengthening national pharmacovigilance centres;
- promoting traditional medicine in collaboration with national committees.

The members of the subregional committees should be appointed for a period determined by the national competent authority and the appointment should be renewable for another term. The subregional committee should be composed of experts with collective experience in the following:

- systematic botany;
- pharmacognosy
- pharmacology;
- toxicology;
- haematology;

- galenics;
- internal medicine;
- pharmacy;
- sociology/anthropology;
- drug regulation.

In addition to the above experts, the subregional committees should also have representatives from regional organizations, such as COMESA, ECOWAS, SADC, UMEOUA, as well as the African Drug Regulatory Authorities Network (AFDRAN).

Registration procedure for traditional medicines

The procedure for registering traditional medicines outlined below is intended to serve as a guide to Member States and can be modified, as appropriate, to suit individual country needs. The proposed registration procedure is as follows:

1. An application of intent to register the traditional medicine is addressed to the minister of the health/national/state regulatory authority.

2. The appropriate application form is duly completed and submitted to the national/state regulatory authority along with the following supporting documents:

   (i) Details of the production facility;

   (ii) A copy of the memorandum of understanding, or other form of partnership agreement between the manufacturer and the research institution. This is in order to protect traditional medical knowledge and to ensure that there was mutual agreement between the parties involved in the development of the medicine;

   (iii) Production authorization granted by the national competent authority;

   (iv) Proof of payment of the registration fee as fixed by the national/state drug regulatory authority;

   (v) A proposed price structure of the medicine.

3. Upon satisfactory assessment of the completed application form, a pre-registration inspection of the proposed production facility (ies) is conducted by a team of experts.

4. Samples for laboratory analysis are collected during the pre-registration inspection.

5. Upon satisfactory inspection of the laboratory reports, the brief for the registration of the product is presented to the national expert committee on traditional medicine for consideration.

6. After approval by the committee, the applicant may be required to pay a fixed amount per product for a registration certificate that would be renewable after expiry.

In addition to the steps above, a mechanism for mandatory post-marketing surveillance and reporting on the use of, and adverse reactions to, herbal medicines will be required. Reports should be submitted to the ministry of health (MOH) for authentication and submission to the regulatory authority. As national drug regulatory authority are usually departments of the MOH, reports submitted to the national drug regulatory authority are in fact submitted to the MOH.

The applicant/manufacturer will be required to supply the following information with the application:

- name and full postal address of the applicant (a PO Box Number is not acceptable);
- name and full postal address of the manufacturer of the herbal medicine (a PO Box Number is not acceptable);
- registered premises or marketing outlet (if any);
- site description, company profile and organogram.

Organization of pharmacovigilance

Accelerating the marketing of traditional medicines involves the organization of an efficient system of pharmacovigilance. An indication of safety associated with the long-term use of a traditional medicine does not exclude the existence of specific and chronic toxicity risks. Similarly, the establishment of an efficient warning mechanism is an essential part of the institution of confidence in practitioners of traditional medicine.

Notification system

Traditional health practitioners, health workers and patients constitute the major sources of information about possible adverse effects and reactions to traditional medicines. Data may be collected by national pharmacovigilance centres, using a free telephone system (i.e. a free phone number). This system will complete the notification by sheets from health centres, the communities and traditional health practitioners. Information will also be gathered from health workers by means of standard reporting paper forms because verbal information by phone is subjective and not practical. In the case of the WHO African Region, most patients do not possess

telephones and the pharmacovigilance centres where they exist are short staffed and would need to have records that can be verified and analysed latter. Pertinent data from all sources should be transmitted to national or state drug regulatory authorities for collation and processing.

Surveys

A committee of experts and national or state drug regulatory authorities may initiate retrospective or prospective field surveys with a view to verifying certain data associated with pharmacovigilance.

Product authorization and distribution channels

Mechanisms for granting authorizations to produce and distribute traditional medicines should be defined separately for each of the four categories of traditional medicine, as set below. an authorization to practise traditional medicine can cover the production of category 1 traditional medicines. In fact, it is important that traditional health practitioners maintain their capacity to diagnose diseases, prescribe and dispense their remedies. In this regard, the practice of traditional medicine should be regulated under a legal framework capable of defining the medical and legal responsibilities of each practitioner.

Category 1 traditional medicines

As indicated above, an authorization to produce category 1 traditional medicines is covered by a licence to practise traditional medicine. Category 1 traditional medicines should only be available from traditional health practitioners' clinics and herbalists' shops. Ideally, such remedies should not be sold outside the traditional health practitioner's centre, but rather be dispensed strictly by the traditional health practitioner who prepared the remedy.

Category 2 traditional medicines

The production authorization is granted by the national competent authority after obtaining the opinion of the national expert committee. Traditional medicines in category 2 are sold without prescription in pharmacies, community stores and herbalists' shops that are duly recognized by the national/state drug regulatory authority.

Category 3 and 4 traditional medicines

The production authorization is granted by the national competent authority on the basis of the technical opinion obtained from a regional expert committee. Traditional medicines in

categories 3 and 4 are prescribed by a health worker and dispensed only in pharmacies. However, traditional medicines used to treat tuberculosis (TB) may be granted in specialized units offering care and treatment to TB patients. Traditional medicines used in the treatment of HIV/AIDS should only be prescribed by a doctor authorized by the National AIDS Control Programme.

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