Regulatory Situation of Herbal Medicines
A worldwide Review

FOREWORD

Although modern medicine is well developed in most of the world, large sections of the population in developing countries still rely on the traditional practitioners, medicinal plants and herbal medicines for their primary care. Moreover during the past decades, public interest in natural therapies has increased greatly in industrialized countries, with expanding use of medicinal plants and herbal medicines.

The many and various forms of traditional medicinal products have evolved against widely different ethnological, cultural, climatic, geographical, and even philosophical backgrounds.

The evaluation of these products and ensuring their safety and efficacy through registration and regulation present important challenges.

The purpose of this document is to share national experiences in formulating policies on traditional medicinal products and in introducing measures for their registration and regulation, and to facilitate information exchange on these subjects among Member States. The document, at present, only covers 52 countries, but after a few years it will be updated and expanded in the light of experience. Further contributions from governments, institutions, and others would be greatly appreciated.

Dr Xiaorui ZHANG
Traditional Medicine Programme

ACKNOWLEDGEMENTS

The Traditional Medicine Programme acknowledges with special thanks the work of Dr Barbara Steinhoff, Scientist, Bundesfachverband der Arzneimittel-Hersteller e.V. (BAH), Germany in drafting this document, preparing her own original contribution and collating material received from many parts of the world. Thanks are also due to the advisers at WHO regional offices for collecting information from Member States and contributing their comments and suggestions, and to the World Self-Medication Industry (formerly the World Federation of Proprietary Medicine Manufacturers) for collecting information.

Thanks are expressed to Dr Gordon Stott for preparing and editing the final version, and to Mr Guolian Zhang of the WHO Office of Language Services, for assisting in the preparation of the document.

Regrettably, lack of space precludes the naming of all those concerned in the preparation of the document.

REGULATORY SITUATION OF HERBAL MEDICINES
A Worldwide Review

CONTENTS

I. INTRODUCTION

Traditional Herbal Medicines and Human Health

Herbal medicines which formed the basis of health care throughout the world since the earliest days of mankind are still widely used, and have considerable importance in international trade. Recognition of their clinical, pharmaceutical and economic value is still growing, although this varies widely between countries [1].

Medicinal plants are important for pharmacological research and drug development, not only when plant constituents are used directly as therapeutic agents, but also as starting materials for the synthesis of drugs or as models for pharmacologically active compounds. Regulation of exploitation and exportation is therefore essential, together with international cooperation and coordination for their conservation so as to ensure their availability for the future [2].

The United Nations Convention on Biological Diversity states that the conservation and sustainable use of biological diversity is of critical importance for meeting the food, health and other needs of the growing world population, for which purpose access to and sharing of both genetic resources and technologies are essential [2].

Legislative controls in respect of medicinal plants have not evolved around a structured control model. There are different ways in which countries define medicinal plants or herbs or products derived from them, and countries have adopted various approaches to licensing, dispensing, manufacturing and trading to ensure their safety, quality and efficacy [2].

Despite the use of herbal medicines over many centuries, only a relatively small number of plant species has been studied for possible medical applications. Safety and efficacy data are available for an even smaller number of plants, their extracts and active ingredients and preparations containing them [3].

Regulation and Registration of Herbal Medicines

The legal situation regarding herbal preparations varies from country to country. In some, phytomedicines are well-established, whereas in others they are regarded as food and therapeutic claims are not allowed. Developing countries, however, often have a great number of traditionally used herbal medicines and much folk-knowledge about them, but have hardly any legislative criteria to establish these traditionally used herbal medicines as part of the drug legislation.

For the classification of herbal or traditional medicinal products, factors applied in regulatory systems include: description in a pharmacopoeia monograph, prescription status, claim of a therapeutic effect, scheduled or regulated ingredients or substances, or periods of use. Some countries draw a distinction between "officially approved" products and "officially recognized" products, by which the latter products can be marketed without scientific assessment by the authority [2].

The various legislative approaches for herbal medicines fall into one or other of the following categories [2]:

- same regulatory requirements for all products;
- same regulatory requirements for all products, with certain types of evidence not required for herbal/traditional medicines;
- exemption from all regulatory requirements for herbal/ traditional medicines;
- exemption from all regulatory requirements for herbal/ traditional medicines concerning registration or marketing authorization;
- herbal/ traditional medicines subject to all regulatory requirements; and
- herbal/ traditional medicines subject to regulatory requirements concerning registration or marketing authorization.

Where herbal medicines and related products are neither registered nor controlled by regulatory bodies, a special licensing system is needed which would enable health authorities to screen the constituents, demand proof of quality before marketing, ensure correct and safe use, and also to oblige licence holders to report suspected adverse reactions within a post-marketing surveillance system [4].

WHO Policy and Activities

The WHO Traditional Medicine Programme

The World Health Assembly (WHA) has adopted a number of resolutions drawing attention to the fact that a large section of the population in many developing countries still relies on traditional medicine, and that the work force represented by traditional practitioners is a potentially important resource for primary health care. In 1978, the Declaration of Alma-Ata recommended, *inter alia*, the inclusion of proven traditional remedies into national drug policies and regulatory measures.

The policy of the World Health Organization regarding traditional medicine was presented in the Director-General's report on Traditional Medicine and Modern Health Care to the Forty-fourth World Health Assembly 1991, which stated that "WHO collaborated with its Member States in the review of national policies, legislation and decisions on the nature and extent of the use of traditional medicine in their health systems." Based on the relevant WHA resolutions, the major objectives of the Traditional Medicine Programme are: to facilitate the integration of traditional medicine into national health care systems; to promote the rational use of traditional medicine through the development of technical guidelines and international standards in the field of herbal medicine and acupuncture; and to act as a clearing house for the dissemination of information on various forms of traditional medicine.

In resolution WHA42.43 (1989), the Health Assembly urged Member States: to make a comprehensive evaluation of their traditional systems of medicine; to make a systematic inventory and assessment (pre-clinical and clinical) of the medicinal plants used by traditional practitioners and by the population; to introduce measures for the regulation and control of medicinal plant products and for the establishment and maintenance of suitable standards; and to identify those medicinal plants, or remedies derived from them, which have a satisfactory efficacy/side-effect ratio and which should be included in national formularies or pharmacopoeias.

In recent years, many developed countries have shown growing interest in alternative or complementary systems of medicine, with a resulting increase in international trade in herbal medicines and other types of traditional remedies. A stimulus consequently exists, in both developed and developing countries, to assess and rationalize practices, and to control commercial exploitation through over-the-counter sale of proprietary labelled herbal and other "natural" medicines.

Herbal medicines have been included in the International Conference on Drug Regulatory Authorities (ICDRA) since the Fourth Conference in 1986. Workshops on the regulation of herbal medicines moving in international commerce were held at the Fourth and Fifth ICDRA Conferences in 1986 and 1989, both confining their deliberations to the commercial exploitation of traditional medicines through over-the counter labelled products. It was concluded that the World Health Organization should consider preparing model guidelines containing basic elements of legislation and registration [5].

A WHO consultation in Munich, Germany, June 1991, drafted Guidelines for the Assessment of Herbal Medicines which were adopted for general use by the Sixth ICDRA in Ottawa, October 1991 [6]. These guidelines (WHO/TRM/91.4) define basic criteria for the evaluation of quality, safety and efficacy of herbal medicines to assist national regulatory authorities, scientific organizations, and manufacturers to undertake an assessment of the documentation, of submissions and/or the dossiers in respect of such products. A general rule of such assessment is that traditional experience in their use and the medical, historical, and ethnological background of these products shall be taken into account, through detailed descriptions in the medical or pharmaceutical literature or documented accounts of their applications [6].

These guidelines contain basic criteria for the assessment of quality, safety, and efficacy and important requirements for labelling and the package insert for consumers' information. The requirements for pharmaceutical assessment cover issues such as identification, galenical forms, analysis and stability. Safety assessment should at least cover the documented experience of safety and toxicological studies, where indicated. The assessment of efficacy and intended use includes evaluation of traditional use through appraisal of the literature and evidence to support the indication claims. Special chapters on combination products and on requirements for product information for consumers are included. The WHO Guidelines are intended to facilitate the work of regulatory authorities, scientific bodies and industry in the development, assessment and registration of herbal medicines, reflecting scientific results which could be the basis for future classification of herbal medicines and would also accommodate cross-cultural transfer of traditional herbal medicinal knowledge between different parts of the world [6].

In 1994, the WHO Regional Office for the Eastern Mediterranean published Guidelines for Formulation of National Policy on Herbal Medicines [7]. As the majority of the world population seeks treatment with traditional

medical practices, especially herbal medicine, and as herbal medicines are of particular value in gastrointestinal problems, upper respiratory tract ailments, urinary tract diseases and skin diseases, the need to formulate national policies on traditional medicines and to encourage co-operation between Member States in this regard is evident. The aim of such national policies would be to develop regulatory and legal reforms to ensure good practice, and to extend primary health care coverage, while ensuring the authenticity, safety and efficacy of these medicines. Main objectives include the recognition of traditional medicine as an integral part of national health care systems, co-operation between modern and traditional medicine, promotion of the rational use of products, the introduction of quality assurance systems, the guarantee of regular supplies, the promotion of research and development of regulatory measures. It has been recommended to countries that a National Expert Committee be established, which would be the appropriate authority to identify the steps and plans needed to formulate national policy in this area and then to develop, direct and monitor the various phases of its implementation. The functions and activities of the National Expert Committee should include drawing up a national list of essential herbal medicines, preparing guidelines on registration requirements, advising on a national licensing system, advising on means of reporting adverse reactions, and proposing suitable methods of communication and co-operation with the Ministry of Health. Criteria for selection of essential medicinal herbs should be mainly safety, efficacy, health needs and availability for supply. Based on the approved list of medicinal plants of each country, the policy should indicate clearly how the supply of these medicinal plants would be secured. The supply procedure should include collection, cultivation, local production and processing, imports and preservation of the national flora. Within a national quality assurance system, standards and regulations should be set to ensure the quality of all medicinal plants and their preparations that are available in the market. The guidelines contain a special chapter on criteria for research on traditional herbal medicines and on criteria for their rational use [7].

As most herbal medicines still need to be studied scientifically, Member States have been seeking the co-operation of WHO in identifying safe and effective herbal medicines for use in their national health care systems.

To develop criteria and general principles to guide research work on evaluating herbal medicines, the WHO Regional Office for the Western Pacific, in 1992, organized a meeting of experts to develop guidelines for research on herbal medicines. Basic scientific principles and special requirements related to their use in traditional practice are incorporated in these guidelines, the main objectives of which are to ensure their safety and efficacy, to promote their rational use, and to provide research criteria for their evaluation. The guidelines provide a basis for Member States to develop their own research guidelines, and for the exchange of research experience and other information so that a body of reliable data for the validation of herbal medicines may be built up. The adoption of such policy was intended to help to overcome legal barriers against the use of herbal medicines [8].

Research approaches should differentiate between herbal medicines with a long documented experience and those the "traditional" use of which has not yet been established. In accordance with the WHO Guidelines for the Assessment of Herbal Medicines (WHO/TRM/91.4), traditional experience with the respective preparation, which includes long-term use as well as the medical-historical and ethnological background, should be taken into consideration as a general rule in conducting research [8].

Herbal medicines have two special characteristics which distinguish them from chemical drugs; use of crude herbs and prolonged usage. A single herb may contain a great many natural constituents and a combination of herbs even more. Experience has shown that there are real benefits in the long-term use of whole medicinal plants and their extracts, since the constituents in them work in conjunction with each other. However, there is very little research on whole plants because the drug approval process does not accommodate undifferentiated mixtures of natural chemicals, the collective function of which is uncertain. To isolate each active ingredient from each herb would be immensely time-consuming at unsupportable cost, and is almost impossible in the case of preparations.

The summary and recommendations of the Sixth ICDRA prompted WHO to continue to develop pharmacopoeial monographs on herbal medicines on the basis of the Guidelines for the Assessment of Herbal Medicines. In response to the request from Member States, WHO's Traditional Medicine Programme decided to prepare a technical document entitled "WHO Monographs on Selected Medicinal Plants" for primary health care. The information in the monographs includes two parts: Part I consists of summaries of the botanical characteristics, major active chemical constituents and quality control of each plant; Part II consists of summaries of clinical

applications, pharmacology, posology, possible contraindications and precautions, and potential adverse reactions.

A WHO consultation on "WHO Monographs on Selected Medicinal Plants" took place in Munich, Germany 1996. After discussion and review, 28 monographs were adopted. The purpose of this document is: to provide scientific information on the safety, efficacy and quality control of widely used medicinal plants; to facilitate the proper use of herbal medicines; to provide models for Member States to develop their own monographs on these and additional herbal medicines; and to facilitate information exchange. The 28 monographs were presented at the Eighth ICDRA meeting in Bahrain, November 1996. Another 32 monographs are being prepared.

II. REGULATORY SITUATION

~~Africa~~

Mali

The Division of Traditional Medicine, a collaborating centre of WHO and recognized by the Organization of African Unity, has started the industrial exploitation of medicinal plants, carrying out activities such as: a survey of practitioners; identification of natural areas of growth of medicinal plants in Mali; botanical, chemical and pharmacological studies; development of improved traditional medicines; improvement of quality control; and training in traditional medicine. Since 1974, associations of traditional therapists have been established [9].

Mauritius

Between 1992 and 1994, a survey was carried out in Rodriguez and Mauritius in the course of a study funded by the European Union under the aegis of the Indian Ocean Commission "Inventory and study of medicinal and aromatic plants of the States of the Indian Ocean". In the course of this study, more than 600 plants entering the traditional pharmacopoeia were identified. The results give a good indication of the distribution and the use of medicinal plants. Phytochemical, botanical, ethno-botanical and bibliographic information is available together with details of physicochemical properties of some additional plants and tests of some of the extracts for their pharmacological properties. Considering the high value of medicinal plants for primary health care, measures for control of this plant material and public information and professional education are required to guarantee the safe and correct use of these products [10].

South Africa

Importance of herbal medicines

A large number of South Africans consult traditional healers, mostly in addition to medical practitioners. There are about 200 000 traditional healers in the country, and indigenous herbal medicines are in the main materia medica. Herbal medicines are also used for self-care.

Legal Status

The trade in crude indigenous herbal products is completely unregulated. However, once a health related