# A. INTRODUCTION

## 1. History of Use of Traditional Herbal Medicines

By definition, 'traditional' use of herbal medicines implies substantial historical use, and this is certainly true for many products that are available as 'traditional herbal medicines'. In many developing countries, a large proportion of the population relies on traditional practitioners and their armamentarium of medicinal plants in order to meet health care needs. Although modern medicine may exist side-by-side with such traditional practice, herbal medicines have often maintained their popularity for historical and cultural reasons. Such products have become more widely available commercially, especially in developed countries. In this modern setting, ingredients are sometimes marketed for uses that were never contemplated in the traditional healing systems from which they emerged. An example is the use of ephedra (= Ma huang) for weight loss or athletic performance enhancement (Shaw, 1998). While in some countries, herbal medicines are subject to rigorous manufacturing standards, this is not so everywhere. In Germany, for example, where herbal products are sold as 'phytomedicines', they are subject to the same criteria for efficacy, safety and quality as are other drug products. In the USA, by contrast, most herbal products in the marketplace are marketed and regulated as dietary supplements, a product category that does not require pre-approval of products on the basis of any of these criteria. These matters are covered extensively in Section 3 below.

### 1.1 The role of herbal medicines in traditional healing

The pharmacological treatment of disease began long ago with the use of herbs (Schulz *et al*., 2001). Methods of folk healing throughout the world commonly used herbs as part of their tradition. Some of these traditions are briefly described below, providing some examples of the array of important healing practices around the world that used herbs for this purpose.

#### 1.1.1 *Traditional Chinese medicine*

Traditional Chinese medicine has been used by Chinese people from ancient times. Although animal and mineral materials have been used, the primary source of remedies is botanical. Of the more than 12 000 items used by traditional healers, about 500 are in common use (Li, 2000). Botanical products are used only after some kind of processing,

which may include, for example, stir-frying or soaking in vinegar or wine. In clinical practice, traditional diagnosis may be followed by the prescription of a complex and often individualized remedy.

Traditional Chinese medicine is still in common use in China. More than half the population regularly uses traditional remedies, with the highest prevalence of use in rural areas. About 5000 traditional remedies are available in China; they account for approximately one fifth of the entire Chinese pharmaceutical market (Li, 2000).

#### 1.1.2 *Japanese traditional medicine*

Many herbal remedies found their way from China into the Japanese systems of traditional healing. Herbs native to Japan were classified in the first pharmacopoeia of Japanese traditional medicine in the ninth century (Saito, 2000).

#### 1.1.3 *Indian traditional medicine*

Ayurveda is a medical system primarily practised in India that has been known for nearly 5000 years. It includes diet and herbal remedies, while emphasizing the body, mind and spirit in disease prevention and treatment (Morgan, 2002).

### 1.2 Introduction of traditional herbal medicines into Europe, the USA and other developed countries

The desire to capture the wisdom of traditional healing systems has led to a resurgence of interest in herbal medicines (Tyler, 2000), particularly in Europe and North America, where herbal products have been incorporated into so-called ‘alternative’, ‘complementary’, ‘holistic’ or ‘integrative’ medical systems.

During the latter part of the twentieth century, increasing interest in self-care resulted in an enormous growth in popularity of traditional healing modalities, including the use of herbal remedies; this has been particularly true in the USA. Consumers have reported positive attitudes towards these products, in large part because they believe them to be of ‘natural’ rather than ‘synthetic’ origin, they believe that such products are more likely to be safe than are drugs, they are considered part of a healthy lifestyle, and they can help to avoid unnecessary contact with conventional ‘western’ medicine.

While centuries of use in traditional settings can be used as testimony that a particular herbal ingredient is effective or safe, several problems must be addressed as these ingredients are incorporated into modern practice.

One problem is that ingredients once used for symptomatic management in traditional healing are now used in developed countries as part of health promotion or disease prevention strategies; thus, acute treatment has been replaced by chronic exposure (e.g., herbal products used for weight loss, Allison *et al.*, 2001). This means that a statement about ‘thousands of years of evidence that a product is safe’ may not be valid for the way

the product is now being used. This does not expressly mean that an ingredient is unsafe; it does mean that safety in the modern context cannot be assumed.

A second problem is that efficacy and effectiveness have rarely been demonstrated using modern scientific investigations. An evidence-based approach to this issue has only recently been implemented, and the results reveal that for most herbal products, considerable gaps in knowledge need to be remedied before one can be convinced about their efficacy.

One of the most difficult issues to contend with in translating traditional herbal practices into conventional 'western' medicine is the individualization of prescriptions containing multiple herbal and other ingredients. There is little incentive for standardization of products for a mass market, when the intention has been to provide an individual prescription. To the small grower or the traditionally trained herbalist, standardization means understanding the growth conditions, the time of harvesting, the manner of extraction or other preparation of material so that a reliable (albeit small amount of) active ingredient can be offered to people. To the manufacturer or distributor of large quantities that will be sold in a supermarket or a health food store, standardization refers to industrial production under defined conditions, using so-called Good Manufacturing Practices (GMP) (Food & Drug Administration, 2002) akin to those used for drug production.

In the USA, there is both small-scale and large-scale production of herbal products and there can be wide variation in their content and quality in the marketplace. Regulations in the USA do not yet require that dietary supplement manufacturers adhere to standard manufacturing practices, and so quality is not guaranteed (see Section 3). The public becomes discouraged by reports that products taken from store shelves do not consistently contain the ingredients — or in the amounts — that are claimed on the label.

For herbal products in common use, evidence of efficacy may be based upon traditional use, testimonials, clinical studies, both controlled and uncontrolled, and randomized, double-blind, placebo-controlled trials. For the most part, however, there is a lack of systematic clinical studies to support claims.

Safety of some herbal ingredients has been recently called into question, in part because of the identification of adverse events associated with their use and, increasingly, because of the demonstration of clinically relevant interactions between herbs and prescription drugs.

Adverse events (stroke, heart attacks, heart-rate irregularities, liver toxicity, seizures, psychoses and death) associated with use of ephedra for weight loss, body-building effects and increased energy or kava-kava (also known as kawa), widely used in Europe and increasingly in Canada to treat anxiety, nervousness, insomnia, pain and muscle tension, for example, have caused some countries to issue regulations restricting or banning these products (e.g. Health Canada Online, 2002a,b). Only a few herbs in common use have been suspected of causing cancer. These include *Aristolochia*, *Rubia tinctorum*, *Morinda officinalis* and *Senecio riddellii*, as discussed in detail below.

# 2. Use of Traditional Herbal Medicines in Developed Countries

## 2.1 Origin, type and botanical data

Plants and their secondary metabolite constituents have a long history of use in modern 'western' medicine and in certain systems of traditional medicine, and are the sources of important drugs such as atropine, codeine, digoxin, morphine, quinine and vincristine.

Use of herbal medicines in developed countries has expanded sharply in the latter half of the twentieth century. Monographs on selected herbs are available from a number of sources, including the European Scientific Cooperative on Phytotherapy (ESCOP, 1999), German Commission E (Blumenthal *et al.*, 1998) and the World Health Organization (WHO, 1999). The WHO monographs, for example, describe the herb itself by a number of criteria (including synonyms and vernacular names) and the herb part commonly used, its geographical distribution, tests used to identify and characterize the herb (including macroscopic and microscopic examination and purity testing), the active principles (when known), dosage forms and dosing, medicinal uses, pharmacology, contra-indications and adverse reactions. Other resources that provide detailed information about herbal products in current use include the Natural Medicines Comprehensive Database (Jellin, 2002) and NAPRALERT (NAtural PRoducts ALERT) (2001). Information about other available databases has been published by Bhat (1995).

## 2.2 Medicinal applications, beneficial effects and active components

In some cases, the active principles of plant-derived products have been isolated and characterized, and their mechanisms of action are understood (e.g., ephedrine alkaloids in some species of *Ephedra*). For many, however, including virtually all of the most common products in the marketplace, such information is incomplete or unavailable. This is in large part due to the complexity of herbal and botanical preparations; they are not pure compounds. It is also a function of the traditionally-held belief that the synergistic combination of several active principles in some herbal preparations is responsible for their beneficial effects.

## 2.3 Trends in use

Data on the global nutrition products industry, in which herbal and botanical products are often included, are given in Table 1.

Sales of dietary supplement products, including herbal and botanical supplements, in the USA increased dramatically during the 1990s, stimulated in the latter part of the

**Table 1. The global nutrition products industry in 1999, including herbal and botanical products (in millions of US $)**

| Country | Vitamins/ minerals | Herbs/ botanicals | Sports, meal replacement, homeopathy, specialty | Natural[a] foods | Natural personal care | Functional foods[b] | Total |
|---|---|---|---|---|---|---|---|
| USA | 7 070 | 4 070 | 4 320 | 9 470 | 3 590 | 16 080 | 44 520 |
| Europe | 5 670 | 6 690 | 2 510 | 8 280 | 3 660 | 15 390 | 42 200 |
| Japan | 3 200 | 2 340 | 1 280 | 2 410 | 2 090 | 11 830 | 23 150 |
| Canada | 510 | 380 | 250 | 700 | 330 | 1 500 | 3 670 |
| Asia | 1 490 | 3 170 | 970 | 710 | 880 | 1 450 | 8 670 |
| Latin America | 690 | 260 | 250 | 460 | 250 | 360 | 2 270 |
| Australia and New Zealand | 300 | 190 | 90 | 340 | 140 | 540 | 1 600 |
| Eastern Europe and Russian Federation | 350 | 220 | 250 | 180 | 40 | 269 | 1 300 |
| Middle East | 180 | 90 | 60 | 70 | 30 | 140 | 570 |
| Africa | 160 | 80 | 70 | 80 | 10 | 120 | 520 |
| **Total global** | 19 260 | 17 490 | 9 960 | 22 700 | 11 020 | 47 670 | 128 470 |

From Nutrition Business Journal (2000), derived from a number of sources. Totals may not add up due to rounding.

[a] Natural foods: foods grown or marketed with a focus on the perceived benefits of 'foods derived from natural sources' and that are, to varying degrees, free of pesticides, additives, preservatives, and refined ingredients

[b] Functional foods: foods fortified with added or concentrated ingredients to improve health and/or performance

decade by the Dietary Supplements Health and Education Act of 1994 (DSHEA) (Tyler, 2000). This pattern of growth has been replicated elsewhere in the world (Table 2), although more recently, sales of herbal products have apparently experienced a decline.

In the European Union (EU), in general, herbal products for which therapeutic claims are made must be marketed and regulated as drugs, while those that do not make such claims may be found in the food or cosmetic categories. Attempts are at present being made to harmonize the scientific and regulatory criteria that govern the marketing of herbal products (AESGP, 1998).

**Table 2. Trends in the global nutrition products industry, 1997–2000 (in millions of US $)**

| | 1997 | 1998 | 1999 | 2000 |
|---|---|---|---|---|
| Vitamins/minerals | 18 000 | 18 870 | 19 620 | 20 440 |
| Herbs/botanicals | 15 990 | 16 980 | 17 490 | 18 070 |
| Sports, meal replacement, homeopathy, specialty | 8 760 | 9 310 | 9 960 | 10 710 |
| Natural foods[a] | 16 690 | 19 910 | 22 700 | 25 420 |
| Natural personal care | 9 620 | 10 280 | 11 020 | 11 850 |
| Functional foods[b] | 40 320 | 43 940 | 47 670 | 51 480 |
| **Total** | 109 380 | 119 290 | 128 470 | 137 980 |

From Nutrition Business Journal (2000), derived from a number of sources
[a] Natural foods: foods grown or marketed with a focus on the perceived benefits of 'foods derived from natural sources' and that are, to varying degrees, free of pesticides, additives, preservatives, and refined ingredients
[b] Functional foods: foods fortified with added or concentrated ingredients to improve health and/or performance

In 1994, when the Dietary Supplements Health and Education Act (DSHEA) was passed in the USA, approximately 50% of the adult population of the country was reported to use dietary supplements and sales of all products combined were approximately $4 billion. This category of products includes vitamins, minerals and a variety of other ingredients; herbal products accounted for about one quarter of those sales. In 2000, the last year for which comparable data are available, again 50% of the adult population reported use of dietary supplements, and sales were close to $15 billion; herbals accounted for nearly one third of those sales. Table 3 identifies some trends in herbal supplement use in the USA from 1997 to 2000.

In the 1990s, the USA saw the growth of government organizations concerned with dietary supplements, such as the National Institutes of Health (NIH) National Center for Complementary and Alternative Medicine and Office of Dietary Supplements, and the National Cancer Institute (NCI) Chemoprevention Program of the Division of Cancer Prevention and Control. Organizations involved with dietary supplements such as the

**Table 3. Ten top-selling herbs in the USA, 1997–2000 (in millions of US $)[a]**

| | 1997 | 1998 | 1999 | 2000 |
|---|---|---|---|---|
| Combination herbs[b] | 1 659 | 1 762 | 1 740 | 1 821 |
| *Ginkgo biloba* | 227 | 300 | 298 | 248 |
| Echinacea[c] | 203 | 208 | 214 | 210 |
| Garlic (*Allium sativum*) | 216 | 198 | 176 | 174 |
| Ginseng[d] | 228 | 217 | 192 | 173 |
| St John's wort (*Hypericum perforatum*) | 100 | 308 | 233 | 170 |
| Saw palmetto (*Serenoa repens*) | 86 | 105 | 117 | 131 |
| Soy (soya) | NA | NA | 36 | 61 |
| Valerian (*Valeriana officinalis*) | 30 | 41 | 57 | 58 |
| Kava-kava | 22 | 44 | 70 | 53 |
| Total herbal supplements | NA | NA | 4 070 | 4 130 |

NA, not available

[a] From Nutrition Business Journal (2001) and Schulz *et al.* (2001). US consumer sales via all channels (includes all retail channels, direct sales, multilevel marketing, mail order and practitioner sales)

[b] Combination herbs include products sold for weight management, athletic performance enhancement or energy enhancement and often include mixtures of several herbal extracts, as well as single-compound ingredients. Others that have appeared in the top 10 list in earlier years, but not in 2000, include: goldenseal (*Hydrastis canadensis*), cranberry, bilberry (European blueberry), aloe (see monograph on *Rubia tinctorum*, *Morinda officinalis* and anthraquinones in this volume).

[c] Two types of coneflower preparation can be recommended and prescribed today: alcoholic extracts made from the root of the pale purple coneflower (*Echinacea pallida*) and juices expressed from the fresh aerial parts of the purple coneflower (*Echinacea purpurea*). It is noteworthy that until about 1990, the root of *Echinacea pallida* appears to have been regularly confused with that of the species *Echinacea angustifolia*.

[d] *Panax ginseng* is cultivated in Asia; *panax quinquefolius* is cultivated in the USA.

American Nutraceutical Association and the Foundation for Innovative Medicine, as well as industry trade associations such as the American Herbal Products Association, the Consumer Healthcare Products Association, the National Natural Foods Association, the Utah Natural Products Alliance and the Council for Responsible Nutrition have been expanding during the 1990s.

In Canada, herbal use has also increased. Berger (2001) noted, in summarizing the results of a 2001 survey of 2500 persons, 15 years of age and older, that herbal remedies were used by 38% of respondents, up from 28% in 1999. A survey in 1998 of the most popular remedies reported in Canada is given in Table 4.

In 1994, the European herbal medicine market was worth over £1.8 billion [US$ 2.8 billion] at retail selling prices. Although the UK market was smaller than that of Germany (in 1994 it was £88 million, compared with £1400 million), it had one of the highest forecast growth rates in Europe (Shaw, 1998).

**Table 4. Top 10 most popular herbal remedies in Canada[a]**

| Herb | % who use among herbal users | % of users in general population |
|---|---|---|
| Echinacea | 54 | 19 |
| Garlic (*Allium sativum*) | 52 | 18 |
| Ginseng[b] | 42 | 15 |
| Camomile (*Chamomilla recutita*)[c] | 38 | 13 |
| *Ginkgo biloba* | 20 | 7 |
| Evening primrose (*Oenothera biennis*) | 20 | 7 |
| Devil's claw (*Harpagoghytum procumbens*) | 17 | 6 |
| St John's wort (*Hypericum perforatum*) | 17 | 6 |
| Tea tree oil (*Melaleuca alternifolia*) | 15 | 5 |
| Valerian (*Valeriana officinalis*) | 13 | 5 |

From Non-Prescription Drug Manufacturers Association of Canada (1998), Sibbald (1999) and Schultz *et al.* (2001)

[a] From a survey of 6849 adults in April 1998

[b] See Table 3.

[c] Reported previously as *Matricaria chamomilla* (WHO, 1999)

The European market for herbal medicinal products was estimated to be worth $5.6 billion at public price level in 1995 (AESGP, 1998).

## 3. Awareness, Control, Regulation and Legislation on Use

### 3.1 WHO guidelines for herbal medicines

In 1992, the WHO Regional Office for the Western Pacific invited a group of experts to develop criteria and general principles to guide research work on evaluating herbal medicines (WHO, 1993). This group recognized the importance of herbal medicines to the health of many people throughout the world, stating: 'A few herbal medicines have withstood scientific testing, but others are used simply for traditional reasons to protect, restore, or improve health. Most herbal medicines still need to be studied scientifically, although the experience obtained from their traditional use over the years should not be ignored. As there is not enough evidence produced by common scientific approaches to answer questions of safety and efficacy about most of the herbal medicines now in use, the rational use and further development of herbal medicines will be supported by further appropriate scientific studies of these products, and thus the development of criteria for such studies'.

The document covered such topics as developing protocols for clinical trials using herbal medicines, evaluating herbal medicine research, guidelines for quality specifications of plant materials and preparations, and guidelines for pharmacodynamic and general pharmacological studies of herbal medicines and for toxicity investigations of herbal medicines.

WHO has also issued Guidelines for the Assessment of Herbal Medicines (WHO, 1996). These guidelines defined the basic criteria for the evaluation of quality, safety and efficacy of herbal medicines with the goal of assisting national regulatory authorities, scientific organizations and manufacturers in assessing documentation, submissions and dossiers in respect of such products. It was recommended that such assessments take into account long-term use in the country (over at least several decades), any description in the medical and pharmaceutical literature or similar sources or documentation of knowledge on the application of a herbal medicine, and marketing authorizations for similar products. Although prolonged and apparently uneventful use of a substance usually offers testimony of its safety, investigation of the potential toxicity of naturally occurring substances may reveal previously unsuspected problems. It was also recommended that regulatory authorities have the authority to respond promptly to new information on toxicity by withdrawing or limiting the licences of registered products containing suspect substances, or by reclassifying the substances to limit their use to medical prescription. The guidelines stressed the need for assessment of efficacy including the determination of pharmacological and clinical effects of the active ingredients, and labelling which includes a quantitative list of active ingredient(s), dosage, and contraindications.

### 3.2 The European Union

The Association Européenne des Spécialités Pharmaceutiques Grand Public (Association of the European Self-Medication Industry; AESGP) has carried out a study for the European Commission on herbal medicinal products in the European Union (EU). The following summary is taken from this report (AESGP, 1998).

The importance of herbal medicinal products varies from one country to another. These products are not a homogeneous group. In general, they are either fully licensed medicinal products with efficacy proven by clinical studies or by references to published scientific literature (in accordance with Article 4.8 a (ii) of Council Directive 65/65/EEC) (European Commission, 1965) or are available as products with a more or less simplified proof of efficacy according to their national use. Many Member States have these two categories, but there are major discrepancies between the Member States in the classification of individual herbal drug preparations and products into one of these categories as well as in the requirements for obtaining a marketing authorization.

### 3.2.1 *Definition of herbal medicinal products*

According to Council Directive 65/65/EEC (European Commission, 1965), which has been implemented in national law in all Member States, medicinal products require prior marketing approval before gaining access to the market. In almost all Member States, herbal medicinal products are considered as medicinal products, and are, in principle, subject to the general regulations for medicines as laid down in the various national medicine laws. In many cases, a specific definition of herbal medicinal products is available, which is in line with the EU Guideline 'Quality of Herbal Medicinal Products'. This includes plants, parts of plants and their preparations, mostly presented with therapeutic or prophylactic claims. Different categories of medicinal products containing plant preparations exist or are in the process of being created. For instance, draft legislation in Spain includes the definitions 'herbal medicinal products' and 'phytotraditional products'. The latter are not considered as 'pharmaceutical specialties' and are therefore not classified as herbal medicinal products.

### 3.2.2 *Classification of herbal products*

Generally, herbal products are classified as medicinal products if they claim therapeutic or prophylactic indication, and are not considered as medicinal products when they do not make these claims. Products not classified as medicinal in most cases belong to the food or cosmetic areas, although they sometimes contain plants which have pharmacological properties. For example, senna pods (from *Cassia* plants, used as laxatives) (see General Remarks and monograph on *Rubia tinctorum*, *Morinda officinalis* and anthraquinones in this volume) can be marketed as food in Belgium. Specific categories of non-medicinal products exist in some Member States, such as the so-called 'therapeutic supplement products' in Austria. In Ireland, Spain and the United Kingdom, there exist preparations defined as medicinal products, which are under specific conditions exempt from licensing requirements.

### 3.2.3 *Combination products*

Herbal ingredients used in combination are widely used in Europe, and their assessment is often performed according to specific guidelines. Combinations of herbal and homeopathic ingredients exist in a few countries. Their assessment follows rather strict criteria, usually those of a 'full' application procedure. Combinations of herbal ingredients and vitamins are available in many countries.

### 3.2.4 *Documentation of quality, safety and efficacy*

A marketing authorization for a herbal medicinal product is, in principle, granted based on an extensive dossier in terms of proof of quality, safety and efficacy in all Member States, with the exception of Denmark and Finland, where it is possible to use

only references to published data for herbal medicinal products. Luxembourg, in practice, only grants marketing authorization based on the assessment of other countries. In principle, according to Article 4.8 (a) (ii) of Council Directive 65/65/EEC (European Commission, 1965), the option of using reviews on published data is available in all Member States. However, this 'bibliographical' option is sometimes only available through assessment on a case-by-case basis or not used in practice. Austria permits this type of application for safety documentation only.

### 3.2.5 *ESCOP and WHO monographs*

European Scientific Cooperative on Phytotherapy (ESCOP) (see Awang, 1997) or WHO monographs may be used in many Member States as a summary of published data. Many regulatory authorities regard them as helpful documentation for clarifying efficacy and safety.

The European Commission (EC), the EMEA (European Agency for the Evaluation of Medicinal Products) Executive Director and the EMEA Management Board established the EMEA Ad Hoc Group in 1997. This Working Group is made up of representatives from the Member States (primarily health authorities) and representatives from the European Parliament, the EC and the European Pharmacopoeia. The Working Group has reviewed the criteria for the demonstration of quality, pre-clinical safety and clinical efficacy in marketing authorization applications for herbal medicinal products as set out in the Council Directives. The Working Group has proposed requirements for non-clinical testing of herbal drug preparations based on a draft EC Guideline for old substances with long market histories (EMEA, 2000). The Group has also discussed the appropriate role of scientific monographs prepared by the WHO and ESCOP.

### 3.2.6 *Simplified proof of efficacy*

Various traditional herbal medicinal products exist in many Member States in addition to fully licensed herbal medicinal products. For these products, national authorities usually verify the safety and ensure a sufficient level of quality. For proof of efficacy, the level of requirements is sometimes adjusted to take into account the long-term experience and is therefore simplified. For example, a specific simplified procedure exists in Austria, Belgium, France and Germany. Most other countries in the EU do not use this strategy.

### 3.2.7 *Further developed products*

For herbal medicinal products that have been proposed for non-traditional indications or are modified from their traditional form (e.g., highly processed or special extracts), a full licence is required in most cases, and efficacy has to be proven by clinical studies. In several countries, such products are not used.

### 3.2.8 *Individual supply*

Herbal medicinal products (like other medicinal products) are made up and/or supplied to individual patients following a one-to-one consultation between patient and practitioner. Some herbal medicinal products are made according to accepted formulae and are prepared by pharmacists. According to Article 2.4 of Council Directive 65/65/EEC (European Commission, 1965), a marketing authorization is not needed. A specific situation exists in the United Kingdom, where a practitioner, according to Section 12 of the Medicines Act 1968 (Griffin, 1998), may supply products to a customer without a licence.

### 3.2.9 *Products from foreign countries*

The quality of imported medicinal plants and their preparations is assessed differently in different Member States. In some cases, no specific regulations exist concerning the control of raw materials or crude drugs, particularly for products that enter the market as foodstuffs or other products that are not controlled in the same way as medicinal products. Finished products are often treated as new chemical entities with full proof of quality, safety and efficacy being required.

### 3.2.10 *Good manufacturing practices and quality control*

All Member States apply the manufacturing requirements of Council Directive 75/319/EEC (European Commission, 1975) to herbal medicinal products. Starting materials for herbal medicinal products are in principle controlled in accordance with the European Pharmacopoeia in all Member States. Good manufacturing practice inspections are carried out in nearly all Member States.

The European Pharmacopoeia was created in 1964; its efforts have resulted in the creation of 83 monographs on herbal drugs which are used either in their natural state after desiccation or concentration or for the isolation of natural active ingredients (Council of Europe, 1996).

### 3.2.11 *Post-marketing surveillance*

The adverse reaction reporting systems of the Member States also monitor herbal medicinal products if they are authorized medicinal products. This system has demonstrated its effectiveness in the case of several withdrawals of marketing authorizations for herbal medicinal products due to safety concern in connection with certain plants. Consumer reports could provide a picture of the spectrum of adverse reactions to herbal medicinal products and alert authorities to potential problems; the degree of acceptance of such reports varies between Member States.

### 3.2.12 *Advertising, distribution and retail sale*

All Member States have implemented Council Directive 92/28/EEC (European Commission, 1992a) on advertising in national law. This directive covers herbal products if they are authorized as medicinal products.

Wholesale marketing of all medicinal products as well as authorized herbal medicinal products is covered by Council Directive 92/25/EEC (European Commission, 1992b). The retail sale of herbal medicinal products is restricted to pharmacies in Belgium, France, Greece, Ireland, Italy, Luxembourg, Portugal and Spain. It is permitted in other outlets in the case of certain herbal medicinal products in Austria, Denmark, Finland, Germany, the Netherlands, Sweden and the United Kingdom. Distance selling and teleshopping are not permitted for herbal medicinal products in most countries.

### 3.2.13 *Differences between Member States*

Herbal medicinal products are regarded as medicinal products in most of the Member States and have, in theory, the option of obtaining marketing authorization in the same way as all other medicinal products. However, the legal systems of the Member States differ in the classification of herbal products, in the availability of an application process for a marketing authorization based on a full application, bibliographical application or simplified proof of efficacy, and in the permitted outlets for retail distribution. Member States have different traditions regarding the therapeutic use of medicinal plant preparations, which may make it more difficult for manufacturers of herbal medicinal products to apply for marketing authorization using the decentralized procedure.

## 3.3 **Individual countries** (Calixto, 2000)

### 3.3.1 *France*

The French Medicines Agency (Agence du Médicament) grants marketing authorizations based on abridged dossiers by making reference to traditional use. The shortened procedure requires limited or no pharmacological, toxicological and clinical tests and is detailed in the Agency Instructions No. 3. The list of drugs with accepted traditional uses was first published in 1985 by the Ministry of Health and has subsequently been revised several times (Table 5). Traditional use of approximately 200 herbal drugs or preparations derived from these drugs has been recognized for minor indications. Agency Instructions No. 3 includes rules for labelling and packaging of herbal medicinal products. If the drug is not specifically included in the list, there is no option to use an abridged procedure (AESGP, 1998). As of 1997, local medicinal plants were on the A list of the French Pharmacopoeia (Castot *et al.*, 1997) which groups the 454 herbs which benefit/risk ratio is considered as positive when traditionally used.

**Table 5. Examples of plants and indications from the French Agency Instructions No. 3 (*Cahiers de l'Agence No. 3*) (Agence du Médicament)**

| Medicinal plant | Information for the medical profession | Information for the public |
|---|---|---|
| *Valeriana officinalis* | Traditionally used in the symptomatic treatment of neurotonic conditions of adults and children, notably in cases of mild sleeping disorders | Traditionally used to reduce nervousness in adults and children, notably in case of sleeping disorders |
| *Matricaria chamomilla* | Traditionally used topically as a soothing and antipruriginous application for dermatological ailments and as a protective treatment for cracks, grazes, chapped skin and insect bites. | Traditionally used topically as a soothing application and to calm the itching of skin ailments and in cases of cracks, grazes, chapped skin and insect bites. |
| | Traditionally used in the symptomatic treatment of digestive upsets such as epigastric distension, slow digestion, eructation and flatulence. | Traditionally used to promote digestion. |
| | Traditionally used to stimulate appetite. | Traditionally used to stimulate appetite. |
| | Traditionally used in cases of eye irritation or discomfort due to various causes (smoky atmospheres, sustained visual effort, swimming in the sea or swimming baths, etc.). | Traditionally used in cases of eye irritation or discomfort due to various causes (smoky atmospheres, sustained visual effort, swimming in the sea or swimming baths, etc.). (Precaution: use only for mild conditions. If the symptoms increase or persist for more than two days, consult a doctor). |
| | Traditionally used locally (mouth and throat washes, lozenges) as an analgesic in conditions of the oral cavity and/or larynx. | Traditionally used for the temporary relief of sore throat and/or transient hoarseness. |
| *Cassia senna*[a] | Short-term treatment of occasional constipation. | This medicinal product is a stimulant laxative; it stimulates bowel evacuation. It is intended for the short-term treatment of occasional constipation. |
| *Hypericum perforatum* | Traditionally used topically as a soothing and antipruriginous application for dermatological ailments and as a protective treatment for cracks, grazes, chapped skin and insect bites. | Traditionally used topically as a soothing application and to calm the itching of skin ailments and in cases of cracks, grazes, chapped skin and insect bites (Precaution: do not use before exposure to the sun). |
| | Traditionally used for sunburn, superficial burns or small area and nappy rash. | Traditionally used for sunburn, superficial burns or small area and nappy rash (Precaution: do not use before exposure to the sun). |
| | Traditionally used locally (mouth and throat washes, lozenges) as an analgesic in conditions of the oral cavity and/or larynx. | Traditionally used for the temporary relief of sore throat and/or transient hoarseness. |

**Table 5 (contd)**

| Medicinal plant | Information for the medical profession | Information for the public |
|---|---|---|
| *Plantago major* L. | Traditionally used topically as a soothing and antipruriginous application for dermatological ailments and as a protective treatment for cracks, grazes, chapped skin and insect bites. | Traditionally used topically as a soothing application and to calm the itching of skin ailments and in cases of cracks, grazes, chapped skin and insect bites (Precaution: do not use before exposure to the sun). |
| | Traditionally used in cases of eye irritation or discomfort due to various causes (smoky atmospheres, sustained visual effort, swimming in the sea or swimming baths, etc.). | Traditionally used in cases of eye irritation or discomfort due to various causes (smoky atmospheres, sustained visual effort, swimming in the sea or swimming baths, etc.). (Precaution: use only for mild conditions. If the symptoms increase or persist for more than two days, consult a doctor). |

From AESGP (1998)
[a] See General Remarks

Castot *et al*. (1997) have reviewed the surveillance or pharmacovigilance of herbal medicines in France. Between 1 and 15 October 1996, the authors observed 15 publications or publicities in 23 magazines widely available in France; these publications/ publicities offered for sale by mail a number of medicinal plants found or not found on the list of 34 'approved' plants. (These plants were listed in 1979 by the government in reason of lack of reported toxicity in traditional use or following complete bibliographic investigation.)

Between 1985 and 1995, the French national surveillance system registered 341 cases of undesirable effects possibly linked to herbal medicines; this figure represents only 0.35% of the total adverse effects from all drugs reported during the same period. The number of adverse effects from herbal medicines is almost certainly under-reported. The population concerned was largely female (73%) with a mean age of 50 years; reasons for taking herbal medicines were constipation, obesity and anxiety. Undesirable effects reported were quite diverse, including allergic and cutaneous responses, eczema, liver damage (linked to germander (*Teucrium chamaedrys*, tonic, diuretic)), digestive problems (linked to laxative plants), neurological effects such as vertigo (linked to plants classified as sedatives) and blood pressure fall and hypokalaemia (linked to plant laxatives containing anthraquinones (see monograph in this volume)). Outcome of these cases was generally favourable (Castot *et al*., 1997).

### 3.3.2 *Germany* (see Kraft, 1999; Calixto, 2000)

Keller (1991) summarized the legal requirements for the use of phytopharmaceutical drugs in the Federal Republic of Germany. The legal status for herbal remedies was defined by the Medicines Act of 24 August 1976. For finished drugs a marketing authorization is obligatory. Herbal finished drugs have to comply with the same criteria for quality, safety and efficacy as all other finished drugs. Finished herbal drugs may be authorized for marketing in one of three ways:

(i) *Evaluation and validation of old medicines*. Finished drugs registered in 1978 possessed a provisional marketing authorization and could remain on the market until the end of April 1990. The medical evaluation of these drugs was mainly based on published data and was carried out by a special expert committee, the Commission E (Expert Commission for Herbal Remedies). The preparation of new monographs by Commission E ended in 1993 (Sandberg & Corrigan, 2001).

(ii) *Standardized marketing authorization*. Medicines that do not represent a direct or indirect risk for health can be exempted from the need for an individual marketing authorization by reference to a previously existing monograph.

(iii) *Individual application for marketing authorization.* In this procedure, complete documentation including the results of analytical tests, results of pharmacological and toxicological tests and results of clinical or other medical tests are required.

In addition, drugs sold outside pharmacies and only for traditional uses without clinical evidence for efficacy have to be labelled as ‘traditionally used’ (Table 6).

### 3.3.3 *United Kingdom*

A number of papers have discussed the situation regarding herbal medicines in the United Kingdom. De Smet (1995) recommended that herbal products be licensed as special products ‘medicines’; he estimated that unlicensed preparations accounted for over 80% of herbal sales. Many medicine-like products on the British herbal market remain unregistered for two reasons: acceptable data on efficacy, safety and quality may not be available, and the licensing fee is high. Traditional experience with herbs can be a useful tool in detecting acute toxicity, but is less useful in detecting rare adverse reactions or those that develop after long-term exposure or after a latent period. Therefore, traditional experience needs to be supplemented with orthodox data from research and post-marketing surveillance. Such post-marketing surveillance is only partly helpful, as herbal suppliers and traditional practitioners are not obliged to report suspected adverse reactions and herbal products are of variable quality.

**Table 6. Examples of plants and indications from the German 'traditional' list**

| Active ingredients | Dosage form | Indication 'Traditionally used for …' |
|---|---|---|
| Ginseng root (liquid extract prepared with wine) | Liquid for oral administration | Improvement of the general condition |
| St John's wort (aqueous liquid extract) | Liquid for oral administration | Improvement of the condition in case of nervous stress |
| Garlic + mistle herb + hawthorn flowering tops | Sugar-coated tablets | Support of cardiovascular function |
| Garlic oil | Gastro-resistant capsules | For prevention of general atherosclerosis |
| Hamamelis leaf (aqueous liquid extract) | Cream | Support of skin function |
| Ginger + juniper berries | Tables | Support of digestive function |
| Onion (oily viscous extract) | Capsules | Prevention of general atherosclerosis |
| Melissa leaf | Sugar-coated tablets | Improvement of the condition in case of nervous stress, for support of stomach function |
| Dandelion root (aqueous solid extract) | Capsules | Support of the excretory function of the kidney |

Adapted from AESGP (1998)

Shaw (1998) has discussed the safety aspects of herbal remedies in the United Kingdom. The legal status of herbal remedies/medicines in the United Kingdom can be broadly divided into three categories:

(i) Most herbal products are unlicensed and therefore no medicinal claims can be made. These are regarded as food supplements and come under food legislation (Ministry of Agriculture, Fisheries and Food (MAFF), 1998).
(ii) Licensed medicinal products require evidence of quality, safety and efficacy and are regulated by the Medicines Control Agency.
(iii) Herbal medicines supplied by a herbalist are exempt from licensing under the 1968 Medicines Act.

Since 1996, the Medicines Control Agency has included adverse reaction reports on unlicensed herbal remedies within its remit and now monitors all three categories (Griffin, 1998).

The House of Lords Science and Technology Committee in early 1999 reviewed a large amount of oral and written evidence from a wide variety of sources in order to scrutinize complementary and alternative medicine (CAM) including herbal medicines (Mills, 2001). The report noted that public satisfaction with CAM was high and that use of CAM was increasing. Evidence was required that CAM has an effect above and

beyond placebo, and this information needed to be available to the public. The current lack of regulation of CAM did not protect the public interest adequately. Acupuncture and herbal medicine should be subject to statutory regulation under the Health Act 1999, as should possibly non-medical homeopathy. The regulatory status of herbal medicines was viewed as particularly unsatisfactory. The report recommended that training for CAM professionals should be standardized and independently accredited and, for many, should include basic biomedical science. Conventional health professionals should become more familiar with CAM and those working in the best-regulated CAM professions should work towards integration with conventional medicine.

### 3.3.4 *United States*

In the USA, the Food Drug and Cosmetics Act characterizes a product primarily on the basis of its intended use. For a botanical product, this intended use may be as a food (including a dietary supplement), a drug (including a biological drug), a medical device (e.g., gutta-percha) or a cosmetic as shown by, among other things, the products' accompanying labelling claims, advertising materials, and oral or written statements (21 Code of Federal Regulations (CFR) 201.128) (Food and Drug Administration (FDA), 2000).

For products classified as drugs, the FDA regulates them under the authority of the Food Drug and Cosmetics Act and its amendments. Under current regulations, if there is no marketing history in the USA for a botanical drug product, if available evidence of safety and effectiveness does not warrant inclusion of the product in an existing, approved category of OTC (over-the-counter) drugs, or if the proposed indication would not be appropriate for non-prescription use, the manufacturer must submit a new drug application to obtain FDA approval to market the product for the proposed use. If existing information on the safety and efficacy of a botanical drug product is insufficient to support a new drug application, new clinical studies will be needed to demonstrate safety and effectiveness.

Most botanical products in the USA are marketed as dietary supplements. Under the Dietary Supplement Health and Education Act of 1994 (DSHEA), an orally ingested product that meets the definition of a 'dietary supplement' under section 201(ff) of the Food Drug and Cosmetics Act may be lawfully marketed using a statement that (1) claims a benefit related to a classical nutrient deficiency disease (and discloses the prevalence of the disease in the USA); (2) describes how the product is intended to affect the structure or function of the human body; (3) characterizes the documented mechanism by which the product acts to maintain such structure or function; or (4) describes general well-being derived from consumption of the product (section 403 r (6)(A) of the Food Drug and Cosmetics Act, 21 U.S.C. 343 r(6)(A)). The term 'dietary supplement' is defined in section 201 (ff) of the Act and means a product (other than tobacco) intended to supplement the diet that contains one or more of certain dietary ingredients, such as a vitamin, a mineral, a herb or another botanical substance, an amino acid, a dietary

substance for use by people to supplement the diet by increasing the total dietary intake, or a concentrate, metabolite, constituent, extract, or combination of the preceding ingredients (Chang, 1999). A dietary supplement is a product that is intended for ingestion in a form described in section 411C(1)(B)(i) of the Act (i.e., tablet, capsule powder, softgel, gelcap and liquid), which is not represented as conventional food, or as the sole item of a meal or of the diet, and which is labelled as a dietary supplement. It is the responsibility of the manufacturer to ensure that a dietary ingredient used in a dietary supplement is safe for its intended use.

The FDA has issued regulations defining the types of statement that can be made concerning the effect of a dietary supplement on the structure and function of the body. The regulations distinguish these statements from the types of statement that require prior approval as drug claims or prior authorization as health claims.

Safety monitoring of dietary supplements focuses on the post-marketing period. The FDA receives spontaneous reports of suspected adverse events through a variety of means, including through a programme called MEDWATCH, the FDA Medical Products Reporting Program (Goldman & Kennedy, 1998). The post-marketing surveillance system for foods and dietary supplements, called the Adverse Event Reporting Systems, is a passive system that relies on voluntary reporting by concerned parties, primarily health professionals and consumers (AESGP, 1998).

The DSHEA extended the definition of dietary supplements beyond vitamins and minerals and established a formal definition of a dietary supplement using new criteria. The Congressionally mandated Commission on Dietary Supplement Labels (CDSL) suggested that some botanicals may qualify as OTC products under existing statutes; these state that a product may avoid ‘new drug’ premarket approval requirements and may be eligible for marketing under an OTC drug monograph if the product is generally recognized as safe (GRAS) and effective under the conditions for use for which it is labelled and if the product has been used ‘to a material extent and for a material time’ under those conditions. The FDA’s response to the Commission stated that it does not regard marketing experience outside the USA to meet conditions of historical use.

Angell and Kassirer (1998) stated that the primary factor that sets alternative medicine, including its most common form, herbal medicine, apart from conventional medicine is ‘that it has not been scientifically tested and its advocates largely deny the need for such testing’. Angell and Kassirer defined ‘testing’ as the gathering of evidence of safety and efficacy, as required by the FDA. ‘There cannot be two kinds of medicine — conventional and alternative. There is only medicine that has been adequately tested and medicine that has not, medicine that works and medicine that may or may not work. Once a treatment has been tested rigorously, it no longer matters whether it was considered alternative at the outset. If it is found to be reasonably safe and effective, it will be accepted. Alternative treatments should be subjected to scientific testing no less rigorous than that required for conventional treatments’.

### 3.3.5 *Canada*

The Canadian Food and Drug Act and findings of an Expert Advisory Committee on Herbs and Botanical Preparations were consulted by Kozyrskyj (1997) to provide an overview of the issues regarding regulation of herbal products in Canada. Case reports of herbal toxicity were identified to illustrate some of the hazards of herbal products, and references were provided to guide health professionals in searching the literature for clinical trials that have evaluated the efficacy of these drugs.

Herbal products not registered as drugs in Canada are sold as foods and are thus exempt from the drug review process that evaluates product efficacy and safety. An Expert Advisory Committee on Herbs and Botanical Preparations was formed in 1984 to advise the Health Protection Branch (HPB). HPB published lists of hazardous herbal products in 1987, 1989, 1992 and 1993. The last publication elicited a large response from consumers and the herbal industry. As of 1995, the list was still under review (Kozyrskyj, 1997).

The recently formed Office of Natural Health Products (currently the Natural Health Products Directorate) (Sibbald, 1999) is responsible for all regulatory functions including, but not limited to pre-market assessment for product labelling, licensing of manufacturers, post-approval monitoring and compliance and implementation of the recommendations of the standing House Health Committee.

In December 2000, the provincial government of British Columbia approved regulations that established traditional Chinese medicine as an alternative form of primary health care. The cost is not covered under Canadian medicare and practitioners face several practice restrictions. For example, 'no acupuncturist or herbalist may treat an active serious medical condition unless the client has consulted with a medical practitioner, naturopath or dentist or doctor of traditional Chinese medicine, as appropriate' (Johnson, 2001).

### 3.3.6 *Chile*

In 1992 the Unidad de Medicina Tradicional was established with the aims of incorporating traditional medicine with proven efficacy into health programmes and of contributing to the establishment of their practice. Herbal medicines are legally differentiated into: (a) drugs intended to cure, alleviate or prevent diseases; (b) food products for medicinal use and with therapeutic properties; and (c) food products for nutritional purposes (Calixto, 2000).

Herbal products with therapeutic indications and/or dosage recommendations are considered to be drugs. Distribution of these products is restricted to pharmacies. A registration for marketing authorization is needed for herbal products, homeopathic products, and other natural products. An application for such registration consists of the complete formula, the labelling, samples of the product, and a monograph which permits identification of the formula and characteristics of the product (Zhang, 1998).

### 3.3.7 *Japan* (Zhang, 1998; Eguchi *et al.*, 2000; Saito, 2000)

Japanese traditional medicine, as used in Japanese society for more than a thousand years, may be divided into folk medicine and Chinese medicine (or Kampo medicine). Kampo medicine is so popular that the per capita consumption of herbal medicine in Japan seems to be the highest in the world. One hundred and forty-six Kampo drugs are registered as drugs by the Ministry of Health and Welfare (MHW) and are included in coverage under the National Health Insurance. Acceptance of Kampo drugs took place without clinical validation studies. In 1989, about 80% of physicians reported prescribing Chinese medicine. Physicians generally recognize Chinese medicine as a complement to modern medicine; traditional drugs are viewed in Japanese society as safe.

Raw herbs which have long been used as folk medicine and which have also been used for a considerable period as components of an industrial product are each described in a corresponding monograph. These products are freely usable for the purposes indicated in the monograph. Local traditional usage is not sufficient for approval as a drug; the claims and rules of combinations of herbal ingredients are determined on the basis of the pharmacological actions of the ingredients. If a monograph is not available, the claims reported in the Japanese Pharmacopoeia are used as a guide.

In the evaluation of a Chinese medicine, importance is given to 'empirical facts or experience', such as reference data, clinical test reports, etc., rather than the pharmacological action of each ingredient. Safety and efficacy have been estimated based on general methods employed by modern medical science. In 1972 the MHW designated 210 formulae as OTC drugs; this selection was based primarily on the experience of doctors actually practising traditional Chinese medicine. In 1976, the MHW specified 146 formulations as 'National Health Insurance (NHI) applicable prescription drugs'. In the case of an application for approval of a prescription drug other than those previously listed, specified data on safety, stability, comparison with other drugs, clinical test results, etc. must be submitted.

New Kampo drugs are regulated in essentially the same way as 'western' drugs in Japan. The same data required for new 'western' drugs are required for new Kampo drugs, including data from three-phase clinical trials.

Since 1971, the MHW has been running a programme for re-evaluation of all drugs marketed before 1967; a new system to re-evaluate the efficacy and safety for all drugs every five years was launched in 1988.

An Advisory Committee for Kampo drugs was established in 1982 in close association with the MHW in order to improve quality control of Kampo drugs. Since the 1986 Good Manufacturing Practice Law, the standard applied to all pharmaceutical drugs has also applied to Kampo drugs. In addition, in 1985, guidelines for ethical extract products in oriental medicine formulations were developed.

The MHW has three major systems for collection of adverse reaction data. The first is a voluntary system involving 2915 monitoring hospitals. The second system — the Pharmacy Monitoring System — which includes 2733 pharmacies, collects data on cases

of adverse reactions to OTC drugs. The third system is Adverse Reaction Reporting from Manufacturers. These cases are reported to the MHW by the responsible company, with information arising from medical conferences and from journals.

### 3.3.8 *Korea (Republic of)*

The Pharmaceutical Act of 1993 explicitly allowed pharmacists to prescribe and dispense herbal drugs (Cho, 2000).

### 3.3.9 *China*

Many herbal medicines have been used for hundreds of years and it is assumed in many cases that they must work. For example, about 7000 species of plants are used in China as herbal medicines, but only 230 of the most commonly used ones have been subject to in-depth pharmacological, analytical and clinical studies.

The 2000 edition of the Chinese pharmacopoeia included 784 items on traditional Chinese medicines and 509 on Chinese patent medicines. Herbal medicines in China are normally considered as medicinal products with special requirements for marketing. New drugs have to be investigated and approved according to the Drug Administration Law. New traditional Chinese medicines are classified under five categories based on the Amendment and Supplement Regulation of Approval of new traditional medicines:

*Class 1*

(1) Artificial alternatives of Chinese crude drugs.
(2) Newly discovered Chinese crude drugs and their preparations.
(3) Active constituents extracted from Chinese crude drugs and their preparations.
(4) Active constituents extracted from a composite formulation of traditional Chinese medicines.

*Class 2*

(1) Injection of traditional Chinese medicines
(2) Use of new medicinal parts of Chinese crude drugs and their preparations.
(3) Effective fractions extracted from Chinese crude drugs or natural drugs and their preparations.
(4) Chinese crude drugs artificially developed in an animal body and their preparations.
(5) Effective fractions extracted from a composite formulation.

*Class 3*

(1) New composite formulations of traditional Chinese medicines.
(2) Composite preparations of traditional Chinese medicines and chemical drugs with the main efficacy due to the traditional Chinese medicine.
(3) Domestically cultivated or bred crude drugs originally imported and commonly used in China, and their preparations.

*Class 4*

(1) Preparation with a change of dosage form or route of administration.
(2) Botanical crude drugs acclimatized from their origin, or crude drugs from a domesticated wild animal in China.

*Class 5*

Marketing drugs with new indications or syndromes.

In Hong Kong in 1989, the Government appointed a Working Party to review and make recommendations for the use and practice of traditional Chinese medicines. In 1995 the preparatory Committee on Chinese medicines was formed to manage the implementation of these recommendations: as a result 31 potent Chinese medicines that may potentially cause adverse effects have been identified. Proprietary preparations containing a combination of herbal ingredients and conventional drugs are regulated in the same manner as other conventional drugs.

The majority of suppliers are state-owned or state-connected. The extensive pharmacopoeia relating to traditional Chinese medicine allows the parallel manufacturing and sale of both pharmaceutical drugs and traditional herbal blends (Chan, 1997; Zhang, 1998).

### 3.3.10 *Saudi Arabia*

Registration of medicinal products by the Ministry of Health is obligatory, as is that of products, in addition to drugs, with medicinal claims or containing active ingredients having medicinal effects such as herbal preparations, health and supplementary food, medicated cosmetics, antiseptics or medical devices (Zhang, 1998).

### 3.3.11 *South Africa* (Zhang, 1998)

The trade in crude indigenous herbal products is completely unregulated. A large number of South Africans consult traditional healers, generally in addition to medical practitioners. There are about 200 000 traditional healers in the country.

Once a health-related claim is made for a finished herbal product, that product must go through a full drug evaluation in the Medicines Control Council (MCC) before marketing.

Specific regulations for registration and control of new ‘traditional’ herbal medicines do not exist. Old medicines, including such well known herbal medicines as senna or aloe, are already registered by the MCC, according to internationally accepted standards of efficacy and safety. Pharmaceutical standards need to be consistent with those of the United States Pharmacopeia or the British Pharmacopoeia.

3.3.12 *Australia and New Zealand* (Moulds & McNeil, 1988; Zhang, 1998)

*The Therapeutic Goods Act 1989* sets out the legal requirements for the import, export, manufacture and supply of medicines in Australia. It details the requirements for listing or registering all therapeutic goods in the Australian Register of Therapeutic Goods (ARTG), as well as many other aspects of the law including advertising, labelling and product appearance. Australian manufacturers of therapeutic goods must be licensed and their manufacturing processes must comply with the principles of Good Manufacturing Practice (GMP). All medicines manufactured for supply in Australia must be listed or registered in the ARTG, unless they are specifically exempt or excluded. Listed medicines are considered to be of lower risk than registered medicines. Most complementary medicines (e.g., herbal, vitamin and mineral products) are examples of listed products. Medicines assessed as having a higher level of risk must be registered (not listed). Registered medicines include non-prescription (low-risk, OTC) medicines and prescription (high-risk) medicines. Complementary medicines (also known as 'traditional' or 'alternative' medicines) include vitamin, mineral, herbal, aromatherapy and homeopathic products. Complementary medicines may be either listed or registered, depending on their ingredients and the claims made. Most complementary medicines are listed in the ARTG and some are registered (Therapeutics Good Administration, 1999).

In New Zealand, supplements in the market place are largely manufactured in the USA. Regulations are not restrictive; there are no limits on ingredients or potencies and 'structure/function' claims are allowed.

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