

The Association of the European Self-Medication Industry

37th Annual Meeting

**“Access to Self-Care:
The Revolution is Here!”**



Rome, Italy – 6-9 June 2001

Special Conference Report – Part 2

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FOOD SUPPLEMENTS, FORTIFIED FOOD AND HEALTH CLAIMS: WHAT ARE THE GLOBAL PERSPECTIVES?

Chairman's introduction

In his introduction, **Mr Bernd van Till**, Chair of the AESGP Committee on Food Supplements, reminded of the symposium AESGP organised on the topics of food supplements, fortified food and health claims in October 2000. This meeting coincided with the debate in the European Parliament on the Directive on food supplements, which the European Commission had proposed in May 2000. "In the meantime," said Mr van Till, "we have seen a lot of intensive and partly conflictive discussions. Today it is the occasion to benefit from the strong international presence at our annual conference here in Rome and to have a broader look. Not only European but also the global perspective will be discussed, in particular the recent developments in Japan and the United States."

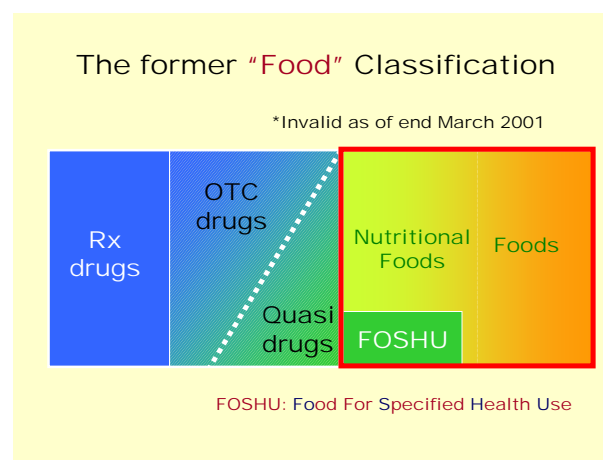
There are many differences between the major markets of the world. However what brings together all the associations dedicated to the area of self-care is a growing interest in the food supplement sector. AESGP therefore installed a specific committee on food supplements in 1998, which brings together multinational companies operating in the sector as well as representatives from national associations, which are often representing a high number of international or nationally operating companies. Through this structure, AESGP has become a leading voice of the manufacturers of food supplements.

This workshop is particularly dedicated to food supplements, but it will also look at issues in relation to fortified food and to the debate around health claims. This session should be seen in close contact with the session which will follow and which is dedicated to the area of herbal medicinal products.

Recent developments in Japan

Mr Akira UEHARA, Chairman of the World Self-Medication Industry (WSMI) and President of Taisho Pharmaceutical Co., Ltd., presented an overview of the current situation and problems of the Japanese health food market.

The scope of health food taken in a broad sense expands largely into the area of food. Taken in a narrow sense, the border between health food and medicinal products will become an issue, said Mr Uehara. He presented the Japanese Health Food Market with viewpoints as close as possible to "Dietary Supplements" in the U.S., "Food Supplements" in Europe and "Complementary Medicines" in Australia. In this sense, it resembles the market made up till the end of March 2001 by the category of so-called "Nutritional Foods" in Japan. The scope becomes more like medicines towards the left side.



Current regulation in Japan

Clear criteria on the classification of food and medicines were introduced in 1971. It is called the 4·6 notification, because it was notified in the 46th year under the Showa era, which is 1971. It can be summarised in the following 4 points:

1. Ingredients
2. Indications
3. Directions to use
4. Dosage forms

The Health Food market was controlled under this regulation for a long time, but recently there were two meaningful revisions of the regulations concerned.

Influential Regulations of Foods

1. Deregulation of dosage forms (2000)

“Office of Trade and Investment Ombudsman” (OTO)

↓ Reflecting the opinions

- Complete abolition of any restrictions on food dosage forms
- Round tablets and capsules are available to foods

One was the deregulation of dosage forms. In the past, the use of drug-like dosage forms such as round tablets and capsules were basically forbidden for foods. However, reflecting the opinions of the “Office of Trade and Investment Ombudsman” - which can directly report to the Cabinet Office - as well as the US regulatory climate – where the DSHEA (Dietary Supplement Health and Educational Act) was adopted in 1994, this restriction was completely abolished in Japan by the year 2000.

Influential Regulations of Foods

2. Introduction of Food For Specified Health Use

FOSHU

FOSHU targets on ;

- Gastrointestinal Condition
- Cholesterol
- Hypertension
- Hyperglycaemia
- Hyperlipemia
- Tooth Caries (tooth cavity, etc)
- Mineral (Ca,Fe) Absorption

The other was the introduction of the category of “Food for Specified Health Use” in 1993 (FOSHU). FOSHU is a health food for which the Minister of Health, Labour and Welfare approves the use of claims that specific functional effects can be expected. However, dosage forms were limited to those that were apparently recognised as a food. As of March 2001, there were approximately 200 approved

products in 12 categories. These products target gastrointestinal conditions, cholesterol levels, hypertension, hyperglycaemia, hyperlipemia and so on.

Examples of FOSHU claims and ingredients

- helps lower the blood **cholesterol** level. (Soy protein)
- suitable for the people with mild **hypertension**. (Lacto-tripeptide)
- suitable for those who require iron supplementation due to their mild **anaemic** condition. (Heme Fe)
- It helps moderate the absorption of sugar. Thus it is suitable for people concerned with their **blood-sugar level**. (Indigestible dextrin)
- It increases intestinal bifidobacteria and thus helps maintain a good **intestinal environment**. (Oligosaccharides)

Typical claims are for example,

- Helps lower the blood cholesterol level
- Suitable for people with mild hypertension.

Reflecting these changes, a new system of Nutritional Foods was announced in April 2001. A series of products vaguely called “Nutritional Foods” in the past were reclassified as “Food with Health Functions” and are divided into two categories.

Food Classification System

Valid from April 2001

	← Food with Health Functions →		
	Rx Drug OTC Drug (Quasi-drug)	Food For Specified Health Use <i>Independently Approved products</i>	Food with Nutrient Functions <i>Standard products</i>
Nutrient contents	?	?	?
Nutrient function claim	?	?	?
Specified Health claim	?	?	?
		↑	
		12 Vitamins and 2 Minerals	

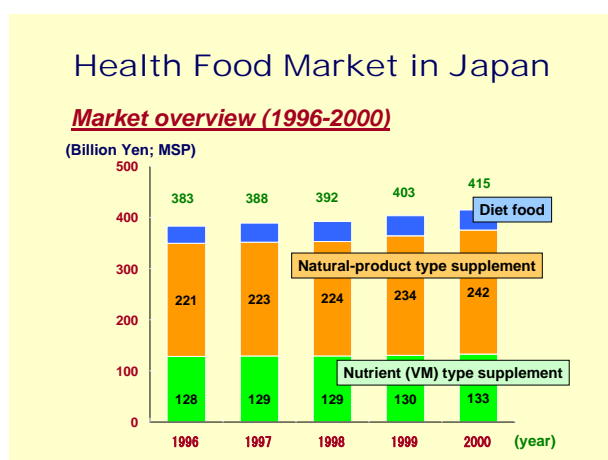
One is the category of “Food with Nutrient Functions” which includes 12 kinds of vitamins and two kinds of minerals, and is allowed to claim nutrient functions.

The other is the category of “FOSHU” mentioned earlier. Only FOSHU among foods can claim the specified health use derived from some designated ingredients, regardless of dosage form. However, to get approval

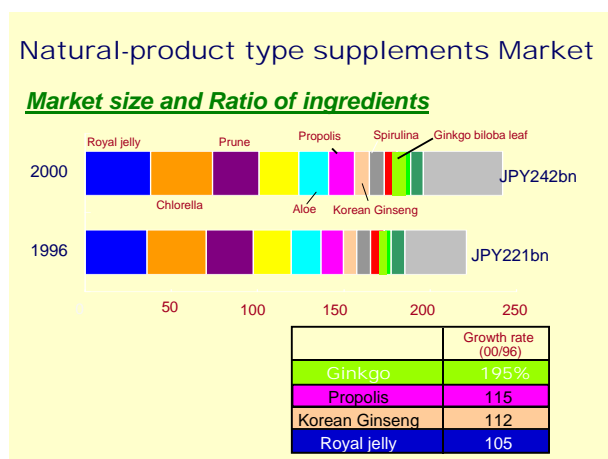
from the authorities, each manufacturer must independently submit scientific data on the efficacy and safety of the food.

The outline of the health food market in Japan

For easier comparison with the markets in Europe, the U.S. and Australia, the Japanese market described here includes supplements such as vitamins, minerals and herbs, and diet foods such as fibres. The total market size in Japan in the fiscal year 2000 was 415 billion yen, broken down as shown in the graph below.

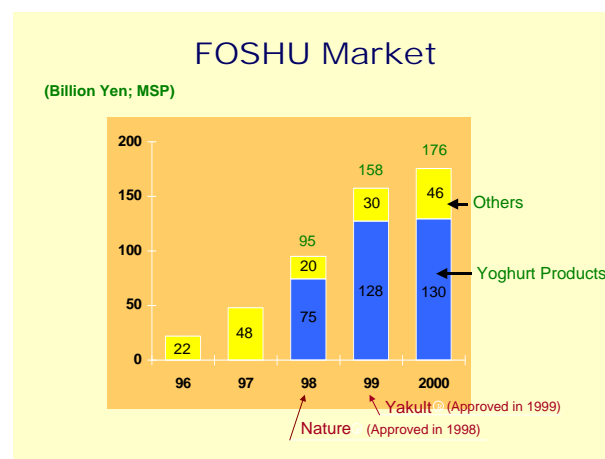


Nutrient-type supplements such as vitamins and minerals tablets accounted for 133 billion yen and natural product-type supplements such as royal jelly, chlorella and herbs capsules accounted for 242 billion yen. Looking at the market trend from 1996 until 2000, sales in 2000 represented an 8% increase over 1996, and a 3% increase over 1999.



Particularly the market of herbs is growing. For example, the market in ginkgo biloba leaves is expanding rapidly and sales represent a 95% increase over 1996.

The total FOSHU market was 180 billion yen in 2000, a surprising 8-fold increase compared with 1996. However, the reason for this rapid growth is due to the approvals, since 1997, of foods that are effective in regulating the intestinal function such as some yoghurt products and Yakult, an intestine-regulating drink.



Features of the health food market in Japan

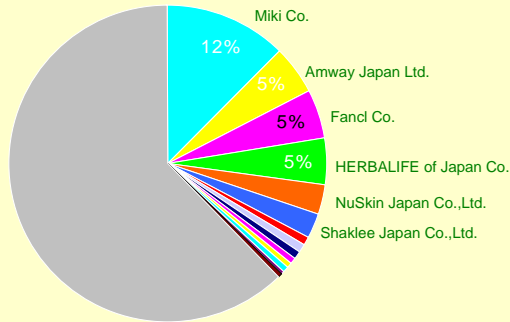
How should a mere 8% growth in the health food market in five years be evaluated? The OTC market in Japan has remained stagnant in the last several years. More than 90% of the consumers recognise that it is their own responsibility to maintain their health. But why do the increasing concern for health and the ageing population structure not result in the direct expansion of Japan's health related businesses? Analysing the features of the health food market from this point of view, the following four points are coming up:

1. Too many manufacturers without established brands

It is said that there are currently 3 000 to 4 000 manufacturers. Under such circumstances, major pharmaceutical manufactures and food manufacturers are trying to get brands established, but they have as yet not gained an overwhelming market share.

- Too many manufactures without established brands

Market share in 2000



- Retail prices of hot-selling line of products are falling

Discount selling of a Vitamin C product

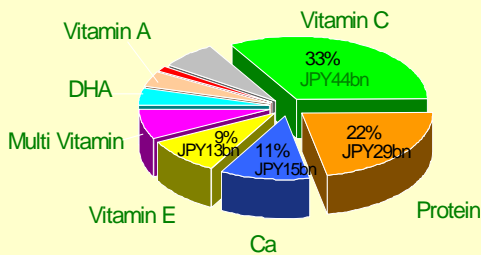


2. Sales are concentrated in single-ingredient products.

70% of the sales of nutrient-type supplements come from vitamin C, protein, calcium and vitamin E products. They are easily understood and accepted by consumers.

- Sales are concentrated in single ingredient products

Sales ratio of single ingredient products in 2000

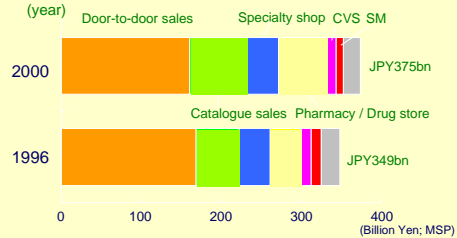


4. The shift from door-to-door to drug-store and catalogue sales

There has been a drastic decrease in door-to-door sales that used to account for 40% of this market. The replacing channels are drug-stores and catalogue sales, where consumers can choose for themselves by themselves. A contributing factor for the increase of catalogue sales has included B2C (business-to-consumer) sales through the Internet.

- The shift from Door-to-door sales to Drug store sales and Catalogue sales

Sales channels of Health Foods (Supplements)



Sales growth rate (00/96)	Dr-to-dr sales	Cat. sales	Specialty shop	Ph./DS	CVS	SM
	95%	133%	101%	157%	88%	73%

3. Retail prices of hot-selling product lines are falling

There is a greater tendency towards discounting for single-ingredient products that are selling well in drugstores with high daily turnovers. For example, the actual retail price of a vitamin C product in drugstores with 1.5 million yen sales on a daily basis is 470 yen, while its recommended retail price is 680 yen and the wholesale price is 400 yen.

Two unresolved problems

When considering the circumstances of the health food market in Japan, two underlying essential problems still remain unresolved. These concern quality and exaggerated advertising. The majority of complaints sent to The National Consumer Affairs Center of Japan (NCAC) and the Japan Consumers' Association (JCA) are related to these problems.

Looking back, it is becoming clear that certain peaks in health food sales have turned out to be just temporary booms. These recurrent booms might have caused consumers to lose trust in the products.

Two problems to be solved

1. Quality

- Product testing (quality check)
by The National Consumer Affairs Center (1999-2000)
 - Pomegranate bark extracts for "Estrogen"
 - Polyphenol products and antioxidation ability
 - Sliming teas: comparison test

2. Exaggerated advertisement

- Some claim medicinal effects illegally on a food
- Related laws and regulations
 - Pharmaceutical affairs law
 - Law for Preventing Unjustifiable Extra or Unexpected Benefit and Misleading Representation

Moreover, the fact cannot be denied that some manufacturers have sold their products through exaggerated advertisements or by intentionally providing misleading information, although these kinds of products are strictly prohibited to claim medical indications and directions.

Summary

In conclusion, the following three issues should be addressed for the future of the health food market in Japan.

1. To foster brands with assured quality, which consumers can trust and support
2. To develop and launch products with high added value based on consumer benefits
3. To offer information and consumer education in order to ensure that consumers continue to purchase with satisfaction.

According to the new system introduced in April this year, new food categories are born, where nutrient functions and specified health use can be claimed. It is expected that major companies – including pharmaceutical companies – will enter this new market. Mr Uehara said he believed it was important that this opportunity was grasped to try to build a better environment for consumers to practise self-care responsibly. "Only when we win the real consumers' trust through such endeavours, can the market continue to grow health-

ily." This is not only valid for the health food market but also for the OTC industry, concluded Mr Uehara. "We need to reconfirm that the 21st century is the age of consumers."

Recent developments in the United States

Mr David SPANGLER, Vice President International Affairs at the Consumer Healthcare Products Association (CHPA), United States, presented recent developments in his country with regard to dietary supplements, as food supplements are called there.

He also touched upon discussions in this area in international bodies such as the Trans-Atlantic Business Dialogue (TABD) and the Codex Alimentarius Committee on Foods for Special Dietary Uses.

Food Supplements, Fortified Food and Health Claims: What Are the Global Perspectives? U.S. Developments

- Starting Points
- Claims
- Quality
- Safety
- Conclusions

Starting Points

- Dietary Supplements: A subset of food
- Definitions drive categorization
 - ☞ "Intended use" key
 - ☞ More than one category possible
 - Same item ☒ 2 categories (supplement-drug, cosmetic-drug, drug-device, etc.)
 - Different items but same main ingredient ☒ 2 categories (cosmetic-drug, drug-pesticide [outside FDA], supplement-food, etc.)
 - **But not** NDAd drugs if not already marketed as dietary supplement or food

– See *Pharmanex v. Shalala*

Starting Points

- Truths and Untruths about the Dietary Supplement Health and Education Act (DSHEA)
 - ☞ Yes, dietary supplements a subset of food. Not drugs (unless ...) Not food additives
 - ☞ No, not "unregulated"
 - ☞ Yes, manufacturer must provide FDA with safety information 75 days before they introduce a new dietary ingredient

Starting Points

- ☞ No, FDA is not the only agency that can act. Federal Trade Commission, state authorities, Consumer Product Safety Commission, others have their own authority
- ☞ Yes, FDA could use more funds to implement their authority

Claims

- Health claims: Pre-approved unless a statement of a scientific authoritative body
 - ☞ Again, food
 - ☞ Typically very 'wordy'
- Pearson v. Shalala: Health claims commercial speech, thus need reasonable fit between regulatory means and policy end

Claims

- Pearson v. Shalala implications: Court wants qualified claims favored over claim prohibitions

Claims

- Structure/function claims
 - ☞ FDA January 2000 rule to provide disease claim v. structure/function claim distinctions
 - ☞ Nutritive value claims a sticking point
- Growing scientific evidence

Quality

- Broad industry support for a GMP regulation
 - ☞ But proposal from FDA when?
- In absence of GMP regulation
 - ☞ USP program in development
 - ☞ AOAC program
 - ☞ National Nutritional Foods Association program
 - ☞ Others

Safety

- FDA activity
- Voluntary labeling programs
 - ☞ Pregnancy/nursing
 - ☞ St. John's wort
 - ☞ Others
- Educational activities
- Reality check on marketplace

Conclusions

- Negative press environment faces industry today
- Growth flat today
- Need GMP regulation
- Want to see FDA better implement its authority
- Encourage growth of scientific evidence

Conclusions

- Codex Committee on Foods for Special Dietary Uses

☞ Will what we see as positive developments in the EU food supplement directive yield better opportunities for agreement?

The perspective of the European Commission

Mr Basil MATHIOUDAKIS, Principal Administrator at the Directorate-General Health and Consumer Protection of the European Commission informed the audience about the latest developments with regard to the European Commission's *Proposal for a European Parliament and Council directive on the approximation of the laws of the Member States relating to food supplements* (published in OJ C311 of 31.10.2000).

Discussions in the European Parliament

This proposal, which the Commission adopted in May 2000, was approved in first reading by the European Parliament on 14 February 2001. The parliamentary Rapporteur on behalf of the Committee on the Environment, Public Health and Consumer Policy was Mrs Emilia Franziska MÜLLER.

In his response to the Parliamentary vote, the European Commissioner responsible for Health and Consumer Protection, Mr David Byrne, informed the assembly which of the adopted amendments to the Commission's original proposal it could accept and where it was not willing to follow Parliament's advice.

Based on this declaration, the European Commission published its *Amended Proposal* for a Directive on food supplements on 19 March 2001 (document COM(2001)159 fi-

nal). The main changes compared with the Commission's original proposal can be summarised as follows.

Two new recitals (8 and 10) were added. Recital 8 said that:

“Specific rules concerning other nutrients or other substances with nutritional or physiological function used as ingredients of food supplements should be laid down at a later stage, provided that adequate and appropriate scientific data about them become available. Until the adoption of such specific Community rules and without prejudice to the provisions of the Treaty, national rules concerning nutrients or other substances with nutritional or physiological function as ingredients of food supplements, for which no Community specific rules have been adopted, may be applicable.”

These intentions were transposed into the text in Article 2:

Article 2.1: For the purposes of this Directive: (a) “food supplements” means foodstuffs that are concentrated sources of nutrients as specified in (b) **or other substances with a nutritional or physiological function**, alone or in combination, marketed in dose form, whose purpose is to supplement the intake of those nutrients in the normal diet;

Article 2.2: **Specific rules on other substances with a nutritional or physiological function shall be laid down at a later stage.**

Recital 10 concerned the evaluation by the Scientific Committee for Food (SCF) of any new substances to be added to the annexes:

“There is a wide range of vitamin preparations and mineral substances used in the manufacture of food supplements currently marketed in some Member states that have not been evaluated by the Scientific Committee for Food and consequently are not included in the positive lists. These should be submitted to the Scientific Committee for Food for urgent evaluation, as soon as appropriate files are presented by the interested parties.” This echoed Commissioner Byrne's declaration before Parliament that the Commission could not accept any additions to the

annexes “in the absence of a positive safety evaluation by the Scientific Committee for Food.” This means that Parliament’s wish to see new ingredients added to the annexes of the proposal could not be implemented with a full evaluation by the EU’s Scientific Committee for Food.

Discussions in the Council of Ministers

Mr Mathioudakis explained that the Council of EU Internal Market Ministers on 30-31 May 2001 was unable to reach political agreement on the European Commission’s amended proposal for a Directive on food supplements. The main outstanding point which prevented the Ministers from reaching agreement were Article 2, which contains the definitions of a food supplement, and Article 5, which deals with the maximum amounts of vitamins and minerals these products would be allowed to contain.

Discussions on these points will continue at the level of the Member States’ ambassadors (the Committee of Permanent Representatives) in September.

[Post-meeting: This will be prepared by a meeting of the attachés on 5 September 2001.

The topic of food supplements is on the agenda of the Internal Market Council of 27 September 2001.]

The perspective of the European Parliament

Mrs Emilia Franziska MÜLLER, the European Parliament’s Rapporteur on the proposal, informed the workshop about the intentions of the various amendments adopted by Parliament in first reading on 14 February 2001. She expressed regret that the Commission was unable to follow Parliament’s opinion in some areas, as shown in the Commission’s amended proposal, and on the apparent deadlock at Council level.

HERBAL MEDICINAL PRODUCTS: WHAT ARE THE GLOBAL PERSPECTIVES?

Recent developments in Canada

Mr David SKINNER, President of the Non-Prescription Drug Manufacturers’ Association of Canada (NDMAC) presented recent developments in Canada in relation with a special category of products now established in Canada called “natural health products.”

Mission Statement



- ◆ To ensure that all Canadians have ready access to Natural Health Products that are safe, effective, and of high quality, while respecting freedom of choice and philosophical and cultural diversity.

Goals and Challenges



- ◆ freedom of informed choice
- ◆ separate regulatory category
- ◆ industry is increasingly innovative
- ◆ market reality (products currently for sale)
- ◆ means to look at entire body of information on a product - standards of evidence
- ◆ general enough to encompass wide range of products
- ◆ specific enough to foster consumer confidence
- ◆ appropriate regulation

Consultations

- ◆ What was done:
 - ◆ distributed over 7000 workbooks
 - ◆ downloaded over 14000 workbooks
 - ◆ answered over 2300 phone calls
 - ◆ visited 11 cities
 - ◆ met with over 2100 participants

Development of the Proposed Regulations

- ◆ Separate NHP regulations under F&D Act
- ◆ Draft of Proposed Regulatory Framework
 - ◆ must address the original goals of the Office
 - ◆ be understandable and in plain language
 - ◆ be appropriate for the various product categories contained within the NHP grouping
- ◆ Supporting NHPD guidance documents

Contents of the Proposed Regulations

- ◆ Definitions
- ◆ Product licensing
- ◆ Site licensing
- ◆ Good manufacturing practices (GMP)
- ◆ Labelling
- ◆ Adverse reaction reporting
- ◆ Appeals mechanism

Definitions

- ◆ Natural Health Product
 - ◆ use: maintain or promote health or prevent or treat diseases or conditions
 - ◆ vitamins, minerals, herbs, homeopathics, traditional medicines
 - ◆ new terms: botanical, animal or micro-organism derived substances, including isolates

Product Licensing (1)

- ◆ All NHPs will be authorized for sale by NHPD and issued a product licence.
- ◆ Two streams:
 - 1) attestation to an NHPD monograph, or
 - 2) submission of other data to support the safety, quality and health claims

Product Licensing (2)

- ◆ NHPD, with assistance from the EAC, is developing standards of evidence
- ◆ Submission data will not be limited to “gold standard clinical trials” but will also include published literature, traditional references, expert opinion reports, etc.
- ◆ Circumstances for the refusal, suspension and cancellation of licenses are proposed, as is an appeals mechanism

Site Licensing

- ◆ Ensures product safety and quality
- ◆ All manufacturers, importers, distributors and packagers selling NHPs in Canada
- ◆ Adherence to GMPs
- ◆ Conditions for the refusal or suspension of a facilities license are proposed, as is an appeals mechanism
- ◆ Questions remain with foreign sites

Labelling (1)

- ◆ Assist consumers, health care providers and retailers in making informed choices about NHPs
- ◆ By knowing:
 - ◆ contents
 - ◆ correct methods for use
 - ◆ merits and limitations of products
 - ◆ any risks associated with use

Labelling ⁽²⁾

◆ Key elements:

- ◆ clear product identity
- ◆ an identification number which indicates market authorization by HC
- ◆ a listing of medicinal and non-medicinal ingredients
- ◆ any cautions, warnings, adverse effects, special storage conditions, etc.

Adverse Reaction Reporting

- ◆ Similar to the one now in place for “drugs”, though slight differences in the relevant definitions
- ◆ All NHP license holders required to monitor and report any serious adverse events to HC

Summary

- ◆ Term “Natural Health Products” important to clear up confusion
- ◆ Regulations based on relative risk and part of health product regulation
- ◆ Level playing field issues important
- ◆ Regulations expected late 2001 or early 2002

Recent developments in Australia

Ms **Juliet SEIFERT**, Executive Director of the Association of the Australian Self-Medication Industry (ASMI) presented recent developments in Australia in the herbal medicines market.

Introduction

In Australia in 2001, Herbal Medicines are regulated under the Therapeutic Goods Act,

1989, and thus are not regulated as foods. In fact, herbal medicine products come under the definition of Complementary Medicines. This definition also includes vitamin, mineral, aromatherapy; and homeopathic products.

These complementary medicines (including herbals) may be further categorised as “registered” or “listed”, depending on their ingredients and the claims made. It is a requirement under the Therapeutic Goods Act, 1989, that sponsors hold information to substantiate all their products’ claims.

Listed Medicines...

- are considered to be **low risk**,
- contain **well-known established ingredients**, usually with a long history of use
- **do not contain scheduled substances** (that are included in the Australian Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP)), and
- are considered appropriate for a degree of self-assessment by their sponsors.

The low-risk profile of these established substances makes it possible to allow sponsors a degree of latitude with these products. To acquire a Listing on the Australian Register for Therapeutic Goods (ARTG) sponsors use what is known as the Electronic Lodgement Facility (ELF). This is a co-regulatory system allowing self-assessment within legislative requirements.

Applications are validated for **quality and safety but not efficacy**.

Registration

If a complementary medicine is not eligible for Listing, it must be **registered**. Registration involves a formal evaluation of **quality, safety and efficacy** by the Office of Complementary Medicines. The Office of Complementary Medicines resides within the Non-Prescription Branch of the Therapeutic Goods Administration.

Registered complementary products are allowed to make **higher level claims**. While a listable may be able to claim *relief* of indiges-

tion, a registrable herbal might be able to support a claim of being a *treatment* for indigestion.

Developments

ELF 3

Currently, the Electronic Lodgement Facility makes use of computer disks that are supplied to sponsors wishing to use the system. Upgrades and changes to the disks in the past have meant that new disks must be provided to sponsors and their agents.

The introduction of version 3 of the Electronic Lodgement Facility (ELF 3) will see the rapid listing of applications shift from a system based on disks to a secure online web browser-based application. In other words, applications will be made directly on a website.

This online application will have the ability to:

- cross reference material and verify information regarding safety and quality within marketing applications for Listed Medicines,
- provide faster access for safer low risk complementary medicines placed on the Australian Register of Therapeutic Goods, and
- further develop and rapidly update the core system data when there are legislative amendments and new low risk substances are approved.

While some in industry were initially wary of an on-line system, fearing higher Internet usage costs or the need to upgrade equipment, most of these concerns have fallen away as the normal passage of time has led companies to make technological upgrades for other reasons.

ELF3 will provide industry with a tool by which it can:

- lodge Listed Medicine applications
- validate information requirements
- gain access to data held by the Therapeutic Goods Administration
- obtain online assistance with applications.

Development issues have seen the introduction of this new system delayed. However, the legislation underpinning the new system has now been passed requiring ELF 3 to be implemented by September 2001.

Post-market surveillance

The introduction of ELF 3 **shifts the emphasis** from pre-market assessment to a more targeted and transparent post-market surveillance program. The areas that receive particular attention under this post-market surveillance regime are:

1. adherence to standards of Good Manufacturing Practice
2. coordinated adverse event reporting
3. agreed testing programs, and
4. identification of unsafe products.

Industry responsibility

While the ELF system increases the speed to market and level of access of herbal and other complementary medicines, it puts a responsibility on industry to ensure that products are manufactured to high standards and that claims are based on sound scientific or traditional evidence. The benefits to industry are that the inherent safety of low risk complementary medicines is maintained in the eyes of the consumer, which ultimately provides both long-term credibility and sustainability for the industry.

Requirements for Levels of Evidence

To build and maintain long-term credibility, the substantiation of claims is key. In Australia, the three agreed principles for claims relating to therapeutic goods are:

- when claiming an intended use or indication, by law, sponsors must hold adequate evidence to support all claims they make about a product;
- claims must be true, valid and not misleading
- claims should not lead to unsafe or inappropriate use of the product.

In order to provide standards for judging the nature of the supporting evidence, a document entitled *Guidelines for Levels and Kinds of*

Evidence to Support Claims for Therapeutic Goods was created. There are two types of acceptable evidence that may be used to support claims:

- scientific evidence, and
- evidence based on the traditional use of a substance or product.

“Traditional use” refers to documentary evidence that a substance has been used for three or more generations for specific health-related and medicinal purposes.

Claim levels

There are three claim levels in Australia:

1. General: allowable in Listed goods – health maintenance, relief of symptoms, claims of traditional syndromes and actions; e.g. for the symptomatic relief of anxiety
2. Medium: allowable in Listed Goods – health enhancement, reduction of a risk and / or aids in the management of a disease / disorder / condition, relief of symptoms of a disease; e.g., may assist in the management of stress disorders
3. High: Registerable goods only – treats / cures / manages / prevents any disease / disorder / condition; e.g., may assist in the treatment of depression.

Joint Herbal Task Force

The Joint Herbal Task Force is an industry / government forum made up of members from ASMI and other industry groups, the Therapeutic Goods Administration, herbalists, manufacturers, academics and growers. The Joint Herbal Task Force considers regulatory and technical issues affecting the herbal medicines industry. It has been said that “a committee is a cul-de-sac down which ideas are lured and then quickly strangled” [Sir Barnett Cocks, 1907], but I assure you that this Task Force is actively addressing the core issues for this sector.

The Joint Herbal Task Force is in the process of considering a Review of the Regulation of Herbal Medicinal Substances. This review is focusing on a number of core issues, such as:

- Definition of ‘herbal substance’ to encom-

pass more traditional low risk preparations such as within Traditional Chinese Medicine

- Clarification on the naming of plant derived substances that do not meet the definition of a herbal substance
- Regulating complex and non-traditional extracts
- Dosages and their implications for safety.

The Task Force is also engaged in a project to try to initiate the development of an industry-funded herbal reference centre using authenticated seeds grown in controlled conditions. This would provide a single national herbal standards reference centre, which industry can utilise as a primary resource for maintaining quality assurance in the identification and supply of herbs.

In conclusion

In Australia, industry actively participates in the on-going development of sustainable and streamlined means of appropriately regulating complementary medicines including herbals.

“ASMI continues to resist the push from some at the margins of our sector to divorce the controls on these products from the schemes already in place for other on-prescription healthcare products making medicinal claims. We are striving for consistency, predictability and transparency that will be in the best interest of the consumer, industry, our industry-funded regulatory body and our National Medicines Policy,” concluded Ms Seifert.

The European perspective

The European perspective was provided by **Dr Konstantin KELLER**, Chair of the Working Party on Herbal Medicinal Products of the European Agency for the Evaluation of Medicinal Products and by **Dr Philippe BRUNET**, Head of Unit, Pharmaceuticals: regulatory framework and market authorisations at the Directorate-General Enterprise of the European Commission.

The Herbal Medicinal Products Working Group

Dr Keller presented the work and current thinking of the Herbal Medicinal Products Working Group which has functioned with the EMEA's structure since May 1997.



His presentation is summarised in the slides below.

Medicine and Culture

Lynn Payer

France: Cartesian Thinking and the Terrain	Great Britain: Economy, Empiricism , and Keeping the Upper Lip Stiff
Germany: The Lingering Influences of Romanticism	United States: The Virus in the Machine

Treatment of Depression by GP

Agence Française de Sécurité Sanitaire des Produits de Santé, July 1998

% of prescriptions in different therapeutic classes 1997
(out of the 10 most relevant therapeutic classes)

	France	UK	Germany
Imipramin-like	16%	36%	35%
SSRI	54%	46%	—
MAO-Inhibitor	—	—	2%
Others	18%	—	—
Phytotherapy	—	—	15%

European Parliament

"[The European Parliament] calls on the Commission to prepare additional proposals on how also to **facilitate the European marketing of herbal** and homeopathic medicines [...]; requests the Commission to **adjust the authorisation procedure** to allow such medicines to be generally available throughout the Community [...], calls for the **setting up of a Traditional Medicines Evaluation Agency**, comprising experts in this field, to assess the worth of phytomedicines;"

(Point 46, Minutes of 16 April 1996, document A4-0104/1996)

WHO 8th ICDRA Bahrain, 10-13 November 1996

Recommendations

... WHO, in collaboration with governments, NGOs, institutions, and collaborating-centres, should continue to develop and review technical documents dealing with herbal medicines, and should **encourage MS to establish groups of experts on herbal medicines in their own countries or regions.....**



EMEA Working Party Herbal Medicinal Products

Delegates and Experts appointed by

Austria	Germany	Netherlands
Belgium	Greece	Norway (2000)
Denmark	Ireland	Portugal
Finland	Italy	Spain
France	Luxembourg	Sweden
		United Kingdom
Eur. Parl.	Eur. Commission	Eur. Pharmac. CVMP (2001)
Hungary	Latvia (2000)	Poland

Mandate of the HMPWG

EMEA Management Board, February 10, 1999

- facilitate **Mutual Recognition** of marketing authorisations in the field of herbal medicinal products;
- creating a **forum for exchange** of experience in the field of herbal medicinal products among Member States;
- **establishment** and regular update of a **common understanding** of exiting legislation and guidelines
- providing **guidance for Competent Authorities and applicants** for the assessment of herbal medicinal products;
- development of **new guidance** on quality, safety and efficacy and of common criteria for interpretation

Report from the EMEA ad hoc Working Group on Herbal Medicinal Products 1997/1998

[Presented to the Management Board on 10 February 1999]

<http://www.emea.eu.int/pdfs/human/hmpwp/002599en.pdf>



The European Agency for the Evaluation of Medicinal Products
Human Medicines Evaluation Unit

Herbal Medicinal Products in the EU Results 2000/2001

Quality guidance documents submitted for scientific review by the QWP and endorsement by the CPMP (December 1999)

Outcome

Guidance on *Good Agricultural and Collection Practice* for starting materials of herbal origin (replaces draft comments on guide for GMP for starting materials and comments on Good Agricultural Practices)

EMEA MB Oct. 2000 / CPMP: discussion with EMEA Inspectors WP May 2001; new HMPWP draft "points to consider" expected July 2001

Herbal Medicinal Products in the EU Results 2000/2001

Quality guidance documents submitted for scientific review by the QWP and endorsement by the CPMP (December 1999)

Outcome

- Note for Guidance on Quality of Herbal Medicinal Products
CPMP/QWP/2819/00 (CVMP/QWP/814/00) draft Nov. 2000 final NiG expected September 2001
- Note for Guidance on Specifications
CPMP/QWP/2820/00 (CVMP/QWP/815/00) draft Nov. 2000 final NiG expected September 2001

Herbal Medicinal Products in the EU Results 2000/2001

Guidance on the assessment of safety

- interactions with Hypericum
ongoing; exchange of information with CPMP PhVWP
- Position paper on the risks associated with the use of aristolochic acid containing medicinal products
submitted to CPMP April 2000, made public October 2000
- risks associated with the use of Sassafras oil / preparations containing Safrole
ongoing; recommendations for national actions
- risks associated with methyleugenol in essential oils
started March 2001, ongoing discussion

Herbal Medicinal Products in the EU

COMMISSION DIRECTIVE 1999/83/EC of 8 September 1999

amending the Annex to Council Directive 75/318/EEC on the approximation of the laws of the Member States relating to analytical, pharmaco-toxicological and clinical standards and protocols in respect of the testing of medicinal products

Official Journal of the European Communities 15.9.1999 L 243/9

Herbal Medicinal Products in the EU

COMMISSION DIRECTIVE 1999/83/EC of 8 September 1999

... (6) Whereas it is in particular necessary to clarify that 'bibliographic reference' to *other sources of evidence* (postmarketing studies, epidemiological studies, studies conducted with similar products, etc.) *and not just tests and trials* may serve as a valid proof of safety and efficacy of a product if an applicant explains and justifies the use of these sources of information satisfactorily ...

Herbal Medicinal Products in the EU

COMMISSION DIRECTIVE 1999/83/EC

(c) Particular attention must be paid to any *missing information* and *justification* must be given why demonstration of an acceptable level of *safety/efficacy can be supported although some studies are lacking*.

Herbal Medicinal Products in the EU

COMMISSION DIRECTIVE 75/318/EEC

Part 3: Toxicological and pharmacological Tests

I. Introduction

The toxicological and pharmacological *tests (bibliographic information)* must show:

- a) the potential toxicity ... and any dangerous or undesirable *toxic effects* that may occur *under the proposed conditions of use in human beings*; ...

Herbal Medicinal Products in the EU Results 2000/2001

Guidance on the assessment of safety

Outcome

Note for guidance on the non-clinical testing of herbal drug preparations with long-term marketing experience - guidance to facilitate mutual recognition and use of bibliographic data

Discussion within CPMP SWP; draft expected 2001

Herbal Medicinal Products in the EU

COMMISSION DIRECTIVE 75/318/EEC

Part 4: Clinical Documentation

Evaluation of the application for marketing authorisation shall be based on clinical trials ((and bibliographic documentation)) including clinical pharmacological trials ((data)) designed ((appropriate)) to determine the efficacy and safety of the product under normal conditions of use, having regard to the therapeutic indications for use in human beings. Therapeutic advantages must outweigh potential risks.

Herbal Medicinal Products in the EU

COMMISSION DIRECTIVE 75/318/EEC

Part 4: Clinical documentation

F. Clinical Efficacy and Safety

8. A **critical assessment** of relative safety, taking into account adverse reactions, shall be made **in relation** to:

- the **disease** to be treated,
- **other therapeutic approaches**,
- **particular characteristics** in sub-groups of patients,
- **pre-clinical data ((information))** on toxicology and pharmacology.

Points to consider on the evidence of safety and efficacy required for well-established herbal medicinal products in bibliographic applications

4. Recognised efficacy

The requirements for ... the documentation required to support the indicated claims should depend on the nature and the level of the indication(s).

For treatment of **minor disorders** a **lower level of evidence** may be adequate, especially when the extent of long-term use, the experience with that particular herbal medicinal product and supportive pharmacological data are taken into account. The level of evidence and the grading of recommendations must correspond to **the nature of the disease** that is to be treated. The **therapeutic alternatives available**, the **risks of a delayed or insufficient treatment** and the **risks of the herbal drug** preparation have to be taken into account.

Grading of Recommendations

Grade A: Evidence Ia, Ib

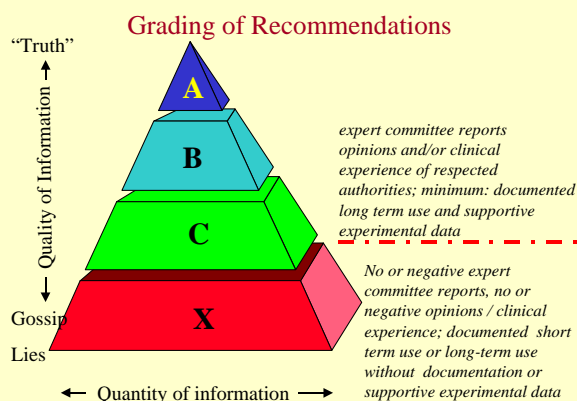
Requires **at least one randomised controlled trial** as part of the body of literature of overall good and consistency addressing the specific recommendation.

Grade B: Evidence IIa, IIb, III

Requires availability of well-conducted **clinical studies but no randomised clinical trials** on the topic of recommendation

Grade C: Evidence IV

Requires evidence from **expert committee reports** or opinions and/or **clinical experience** of respected authorities. Indicates absence of directly applicable studies of good quality



Herbal Medicinal Products in the EU

Guidance on the assessment of safety and efficacy

Assessment of ESCOP/WHO monographs

- 1 final core-SPC (Valerianae radix)
- 8 core-SPCs presented to CPMP (March 2000)
- 7 core-SPCs in discussion within HMPWP
- rapporteur assigned for 28 ESCOP-monographs (March 2001)

Austria: 3	France: 5	Italy: (3)	Sweden: 4
Belgium: 4	Germany: 6	Netherlands: 6	Spain: 2
Denmark: 2	Hungary: 2	Portugal: 5	UK: 2

core-SPC for
Isphagula Husk
(January 1999 - final draft march 2000)
Submission to CPMP March 2000

4.1. THERAPEUTIC INDICATIONS

Herbal medicinal product for

- a) the treatment of habitual constipation; conditions in which easy defecation with soft stools is desirable, e.g. in cases of painful defecation after rectal or anal surgery; (II-III; B)
- b) adjuvant symptomatic therapy in cases of diarrhoea from various causes; (III-IV; C; Decision by Majority)
- c) conditions which need an increased fibre intake, e.g. irritable bowel syndrome. (IIb-III; B; Decision by Majority)

**Draft core-SPC for
Calendula Flower**
(draft March 2000)

4.1. THERAPEUTIC INDICATIONS

Herbal medicinal product for the symptomatic treatment of minor inflammations of the skin (such as sunburn) or the oral mucosa, and as an aid in healing of minor wounds; (IV;C)

**Draft core-SPC for
Devil's Claw Root**
(draft march 2000)
Submission to CPMP March 2000

4.1. THERAPEUTIC INDICATIONS

Herbal medicinal product for the symptomatic treatment of minor articular pain (III-IV;B-C).

The Role of "core-SPCs"

49th Meeting of the Pharmaceutical Committee, March 2000

"The so-called "core-SPCs" (e.g. those elaborated by the Herbal Working Group of the EMEA) are *legally not binding*. The value of these "core-SPCs" is based on their "*persuasive power*", underpinned by the fact that technical experts of all EU competent authorities have considered and agreed upon them."

The Role of "core-SPCs"

Joint Meeting of the Human and Veterinary Pharmaceutical Committees, November 2000

"The intention to **progressively harmonise generic medicinal products** by agreeing upon "core-SPCs" was in general supported by the Member States."

**Draft "core-SPC" for
Hop Strobile**
(draft march 2000)
Submission to CPMP March 2000

4.1. THERAPEUTIC INDICATIONS

None accepted on the basis of bibliographic data provided by the ESCOP monograph. (Decision by Majority)

Traditional Medicinal Products
New legislation - European Commission "Step II"
Provisions of a Directive on traditional medicinal products
October 2000 / April 2001

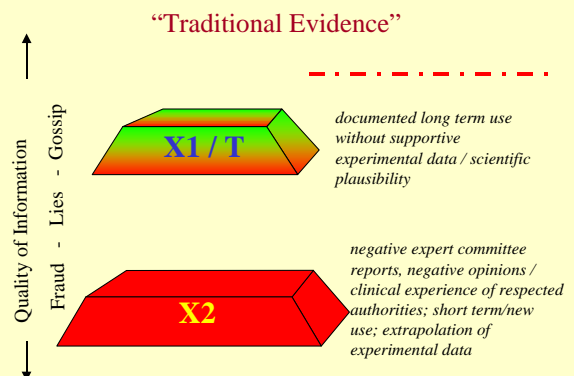
Benefits:

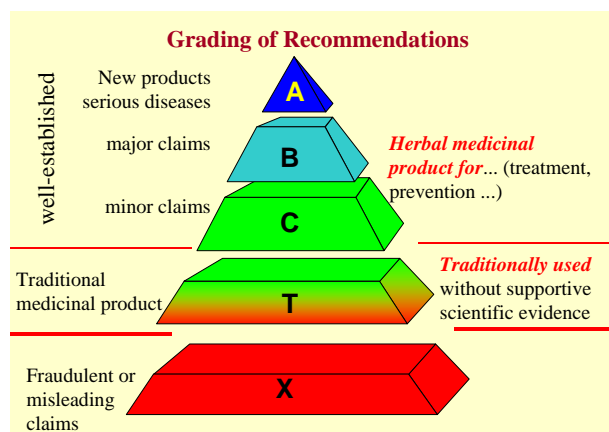
- products with medicinal use classified as medicines
- control of the market
- enforcement of labeling requirements
- GMP applies; clear quality standards, e.g. European Pharmacopoeia
- control of safety
- pharmacovigilance applies

Traditional Medicinal Products
New legislation - European Commission "Step II"

Points for discussion:

- restriction to herbal medicinal products
- definition of "traditional" vs. "well-established" use
- minimum evidence for claims and protection from fraudulent claims
- wording of claims
term "traditionally used in" may be misleading
- products with limited use by ethnic minorities
- national or EU-wide approach
- simple procedure for simple products, e.g. herbal teas





Perspectives

- Herbal medicinal Products are a reality in the European market
- Public Health concerns related to uncontrolled herbal medicinal products and starting material are a reality in the European market
- Lack of Interest in the Industry?
- Mutual recognition of herbal medicinal products not feasible?

Herbal medicinal products with successful MR

TM ®	Year	RMS	CS
Mucivital flavoured (Isphagula husk)	1996	DE	AU; BE; GR; I; PORT; UK
Nozoil (Sesame oil nasal spray)	1997	SE	FI
Minolest (Isphagula husk, Guar gum)	1997	DE	AU; BE; LUX; SE
Valerian Caps. (Valerian root)	1998	UK	AU; GR; I; PORT
Gammaderm (Evening primrose oil cream)	1999	UK	DE; IR
Capsicum Pain Plaster (Capsicum extract)	2000	DE	AU; DK; F; FI; LUX; NOR; SE; UK

Perspectives

Phase of consolidation

- European legislation / Update of procedures
- responsibilities of scientific bodies / centers of excellence
- Implementation of expertise
- Implementation of scientific standards
- Exchange of information and transparency of criteria
- Constant update of standards in the light of experiences gathered by competent authorities and applicants

Future regulation of traditional medicinal products

Dr Philippe Brunet of the European Commission's Pharmaceutical Unit provided an overview of the Commission's recent work on the regulation of traditional medicinal products. The Commission has drafted a text for a Directive on traditional medicinal products which has now been revised and is scheduled to be finally adopted by the European Commission in September 2001.

Dr Brunet explained that this Directive would cover products for which:

- quality requirements will be according to the monographs of the European Pharmacopoeia
- safety requirements can be based on existing data
- fewer efficacy data will be required.

Current Community legislation will be adapted to take account of this new category.

The new Directive, said Dr Brunet, would only cover traditional medicinal products of **herbal** origin. The criteria to determine whether a product could be covered by the new Directive would be:

- The indication: medical intervention should not be required
- The route of administration: only products for oral or external use or for inhalation
- Proof of safety and pharmacological effects would have to be *plausible*.

Traditional medicinal products would have to demonstrate use for a period of 30 years. Part of the proof for this (maximum 15 years) may come from outside the European Union.

HPMWG to become a Committee

The work on the new category of traditional medicinal products would be the responsibility of a new Committee to be set up within the structure of the European Agency for the Evaluation of Medicinal Products (EMA) called the "*Committee for Herbal Medicinal Products*".

The setting up of this Committee is foreseen in the proposals on the revision of the European Union's pharmaceutical legislation to be adopted by the European Commission before the summer.

Future role of the CHMP

The role of the CHMP under the revised legislation would be:

- To establish "herbal monographs" for products covered by Commission Directive 1999/83/EC (covering medicinal products with "well-established use").
- To establish "herbal monographs" for products covered by the planned Directive on

"traditional medicinal products." Dr Brunet specified that these monographs would cover quality and safety. He said that in case a monograph exists for a particular herbal medicinal product, it should be used.

- The CHMP would also have to fulfil further responsibilities conferred upon it by Community under these two Directives.

The Committee will be made up of one member per Member State nominated for a 3-year term which is renewable. Members should be chosen based on their role and experience in the evaluation of herbal medicinal products. They will represent their competent authorities.