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Health Claim on Functional Foods

— Scientific evidence and Proposal for the regulation —

The Second Report
of
Study Committee of Functional Food

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§ 1. Introduction

"Functional food" is a term proposed by the Japanese scientific academy in 1980's, and Japan has been leading other countries in the investigation to frame a system for functional food. In 1991, the term "functional food" was changed to a new term "Foods for Specified Health Use". Legalization was then attempted to notify its efficacy on the label. This is a Japanese government system to approve description of a label regarding an effect of food on the human body for a specific health-related use, which is to be approved by the Minister of Health and Welfare.

Since then, functional food has attracted attention in western countries. The Codex of 1999 proposed "Enhanced Functional Claim" and "Indication of the reduction of the risk of diseases". Currently, discussion is being made as to how we should identify the health-related label as an international standard. Functional food can be understood in its true meaning, both by consumers and manufacturers, only when an appropriate definition is written on the label. Therefore, it is necessary to establish regulations for labeling with regard to scientific evidence. Also, the regulation, which relates with the health related claims, will determine the market scale for each functional food. Legalization for claim of functional food with international consistency and scientific evidence is urged. This is because the needs of functional food are increasing in accordance with the aging society of developed countries including Japan, and it is also due to the growing number of life-style related diseases along with an increase in the health-consciousness of the public and the government policy to reduce medical care cost.

ILSI-Japan has prepared and issued a paper entitled "The current status and problems of Japanese functional food" in 1998 (ILSI; no.55, p18-54, 1998) . After one and half years had passed, the number of Foods for Specified Health Use increased from 100 items to 153* items. The Japanese government also reconsidered the differentiation between foods and drugs to discuss a new system of so-called "dietary supplement". In overseas countries, the policy on the system of functional food is becoming clear in each country, including those described in the Codex. Considering these circumstances, investigation results of domestic and various international situations after the previous report are summarized in this report. Based on the information, we reconsidered the future subjects we had discussed in the previous report, such as problems in differentiation between food and drugs and scientific grounds. We also summarized our ideas in three areas: the description of labeling, an effective system to make the most of the label information, and the responsibilities of the companies.

In the present report, subjects and suggestions are described first, and then the

investigation items and results are described. The subjects for the investigations are based on the information we obtained through July 31, 1999. The investigation results became the base of the scientific grounds for indications in the Item (II) of the § 2 Subjects and Proposals are mentioned in the Item (III) Scientific grounds for the indication of health of the § 3 Investigation Items. And the investigation results of the § 2 - Subjects and Proposal, (III) Proposal for an expression and (IV) Proposal to make the most of the labeling, which became the base for the discussion on the system to better understand the indications, are mentioned in the § 3 Investigation Items, (I) Laws and Regulations. The investigation results mentioned in the § 3 (II) Market are to provide the background for the entire contents of the present report.

* An additional 13 items were approved by November 22, 1999, thus the total approved items increased to 167 as of the end of November, 1999.

§ 2. Subjects and Proposals

(I) Definition of nutrient and non-nutrient

The term "nutrient" can be categorized into the following 4 classifications based on the latest nutrition science:

(1) **Macro-nutrient:** The 3 major components, represented as protein, lipid, and carbohydrate, are categorized as macro-nutrients. These are divided into the structural components that form the body structure and the other components act as the source of energy.

(2) **Micro-nutrient:** Vitamins and minerals are categorized as micro-nutrients. All of the micro-nutrients are essential elements which cannot be replaced by any other components. A small daily uptake of such elements is essential for a smooth life activity, although a part of the minerals are included in the formation of the skeletal structure as mentioned in the macro-nutrient definition.

(3) **Functional non-absorbable non-nutrient:** Components that cannot be absorbed in the body, such as dietary fibers, are included in this category. It affects the bowel movement and its relation with other biological functions has been pointed out.

(4) **Physiologically functional non-nutrient:** Many physiologically active (or bioactive) substances were found except for minerals and vitamins in food according to researches in medicine, pharmacology, and nutrition science. These are necessary for maintenance and improvement of health, and prevention and treatment of diseases due to the recent changes in people's life styles. These changes include new materials for food, dietary life, a progressively increasing elderly population, and the increase of life-style related diseases. This category includes various carotenoids and polyphenols as antioxidant substances, and immunoreactive substances.

In this present report, we define the types of nutrient as follows considering the international agreement (or international harmonization) as described in the codex.

1. Nutrient means the Groups (1) and (2) as mentioned above. However, in Japan, sometimes nutrient necessary for supplementation means vitamins and minerals because the lack of the group (1) is very rare.
2. Non-nutrient means Groups (3) and (4) above. They indicate bioactive substances present in food and components originated in herbs, which are not regarded as nutrients.

(II) Scientific ground for health claim

1. The concept of experimental methods for the scientific basis

1.1 Basic ethical policy on human experimentation (or clinical trial)

The indication on health beneficial effect should be based on the evidence of usefulness, which fulfills safety, and efficacy concerns for humans. Namely, an intervene clinical trial is mandatory to prove the efficacy of the material. This test should show the statistically significant differences in the test results of humans in order to describe the labeling of the given substance. However, in cases where the efficacy of the subject is already scientifically proved, such as by the epidemiological studies and other clinical tests, a discussion is necessary whether to perform additional intervene clinical trials or not to permit its health claim. The epidemiological results are considered insufficient to prove the causal relations compared with those of intervene clinical tests. Therefore, it is natural that high quality is required in the epidemiological data to be the evidence for the indication of effectiveness on health if intervene clinical trials are not performed. It is

very obvious that in cases where an intervene clinical trial cannot be performed because of difficulties due to ethical reasons, another scientifically appropriate test is required to substitute for the intervene clinical trial. Based on these conditions, appropriate health claim should be officially approved in accordance with the quality of the scientific reasons submitted.

The purpose of the intervene clinical trial is to investigate the efficacy and preventive effect for life-style related diseases and the safety of the test food in terms of side effects. Another purpose is to evaluate the usefulness of the test food in the ordinary diet based on the comparative (side effect) evaluation of the test food. The clinical trial should be conducted in a scientifically appropriate manner considering an ethical aspect, since the clinical trial is to be done on humans. It is necessary to evaluate the results of the intervene clinical trial objectively and scientifically in accordance with the policy stated in the Helsinki Declaration. This takes into consideration of protecting test subjects' human rights and guarantees the reliability of test results, in order to ethically and scientifically performs the clinical trial.

The following is our committee outline on the guidelines for clinical trials. The detailed guidelines should be prepared with respect to the methods of the clinical trials for target of health claim group with reference to the opinions of the specialists. It is hoped that this will be used as a reference for the research and development staff after receiving authorization from the official government organization. Also, it is important to include policy regarding the statistical analyses in the guideline. This is in order to apply appropriate statistical analysis methods for the test procedure of human subjects, the methods, the evaluations, and the analysis.

1.2 Proposal regarding clinical trials

1.2.1 Test methods and analysis of the results

Subjective and clear preliminary definition is necessary before the clinical trial to ensure the reliability of the test results. Such preliminary definitions include the study subjects, selection of the subjects, grouping for each test, methods, test period, and evaluation items.

Statistical analyses are necessary to accurately and objectively evaluate the test data. Therefore, special knowledge of statistics is required to form the study plan, to implement it, and to analyze the results. In the report of the test results, the method of statistical analysis should be described.

1.2.2 Implementation of the clinical trial

The clinical trial should be completed with an accurate and consistent method in order to obtain the significant results for scientific evaluation. The clinical trial should be conducted under supervision of a physician subject to approval of an ethical committee.

1.2.3 Study subjects

The study subjects should be selected from appropriate persons that fit the target of the indication of the health effectiveness. The suitability of the subject selection should be discussed in each labeling item for health effect. The subjects, in general, are either healthy subjects, poor health subjects, untreated subjects who have a potential for life-style related diseases, and patients with mild disease who have not been treated. For example, if the target customers are people who have a borderline life-style related disease as defined by medical associations (such as hyperlipidemia and hypertension), the test subject should be from this borderline population rather than healthy people.

In general, pregnant women, suspected pregnant women, or children should be excluded as the test subjects. However, if the indication on the efficacy of health is for such people, the clinical trial should be performed under careful medical considerations.

Human clinical trial required to prove the health indication in Japan should be tested on Japanese subjects. However, clinical trial results of foreign people may be acceptable in cases where racial differences, environmental differences, and eating habit differences are considered inconsequential to the usefulness of the test material.

1.2.4 Clinical trial study design

The study design, in general, needs to include a parallel study*¹ for correct theoretical analysis. However, a crossover method*² is also very useful in cases with a limited subject number.

*¹ A method to allocate different subjects in each test condition for comparison.

*² A method to let all of the subjects experience all of the conditions irrespective of order of the experience.

1.2.5 Test group composition and allocation for the test

In comparative tests, control groups such as untreated groups or placebo groups should be utilized to avoid systematic bias in each test group. Also, use of random sampling is the desired method to ensure (accuracy, fairness and) the comparative grouping with high probability. These methods will provide the scientific base for a statistical analysis.

In general, a double-blind, randomized study*³ is the principle. However, if the double-blind test cannot be applied, or another blind test is difficult to perform, then the reason, an alternative method, and the anticipated effect should be described.

*³ In this method, neither the test subjects nor the researcher in charge of the test know the contents of the test sample. The sampling is randomly chosen.

1.2.6 Number of subjects

The subject numbers should be sufficient to evaluate accurate and objective statistical significance using a statistical method. The subject number is desired to be 10 or more in each group, though the number depends on the study design or the scale of efficacy.

1.2.7 Test food

As a basic principle, the test food is desired to be the final product of the target health indication. However, if the difference between the effective constituents and the final product is very small or if there are other rational reasons, only effective constituents may be sufficient for the test.

1.2.8 Investigation of the dietary life of the subjects

A crucially vital factor is to determine whether the subjects have been eating the test food as prescribed. It is necessary to investigate their eating habits closely. Then, we can clearly decide to continue or discontinue the clinical trial in cases where the subject did not follow all of the rules for the clinical trial.

1.2.9 Analysis method

There is a possibility of incomplete test results; thus not all of the results can be included for the evaluation of the clinical trial. It is necessary to decide the guidelines for each clinical trial regarding whether to include or exclude the incomplete data because they may cause an abnormal inclination during data analysis. Therefore, prediction and policy on the handling of each abnormal case considering the reasons for specific results are required. In general, a statistical analysis is to be performed for evaluation with respect to efficacy, safety, and usefulness. Regarding the major statistical analyses, consideration of the statistical hypothesis and preliminary selection of the appropriate analysis methods to verify the hypothesis are necessary, along with the items subject to analysis. Also, a clear definition of the statistically significant differences, reliability coefficient, and selection of either the two-sided or one-sided test is necessary.

As a basic rule, the two-sample t-test*⁴(or student t-test) is used, and the significance level is defined as 5% or 1%. In the statistical test, the presence of a statistically significant value and the number of variants in each group and along with the probability of significance (p-value)*⁵ should be described.

*⁴ A method to test two independent groups, and is used for parallel group comparison.

*⁵ A probability to support the hypothesis verifying no significant differences between groups. When p-value is below the significant level (5% or 1%), the hypothesis can be withdrawn and be defined as a significant difference.

1.3 Summary

The policies and methods of clinical tests were described above. The important point is to contribute to overall human health by keeping the quality of the test high and to accumulate data for future reference.

As mentioned earlier, it is desired to prepare guidelines for the methods of each clinical trial in each health claim group, to be authorized by the proper government organization, and to be used as a reference of researchers. Also, appropriate application of statistical analyses is crucial in the design, implementation, evaluation, and analysis of human clinical trial subjects. Accordingly, guidelines for statistical analyses of clinical trials need to be prepared.

The physician in charge of the clinical trial, the person who performs the test, and the related committees involved should pay sufficient attention to the human rights and the safety of the subjects. Also, they must recognize that a scientifically accurate decision is important based on the knowledge and experiences of the special field.

2. Proposal of the system and labeling related to scientific evidence

Foods for specified health use (FOSHU) can be interpreted as a food approved to claim a health benefit for showing a specific efficacy on health after intervene clinical test. Based on this idea, the expressions corresponding to the scientific evidence in the clinical test results need to be approved for the health claim of FOSHU. However, the fact is that the health indications, currently approved for specified supplement foods are sometimes indirect and difficult for consumers to understand fully with regard to the significance of their meaning.

The evaluation of anticipated action and efficacy of FOSHU is not for the treatment of diseases as medicine, but improving effect before developing a disease. This includes evaluation of health maintenance and effects which improve one's health condition. With this background, the health labeling of FOSHU has been limited to an indirect expression. However, we suggest reconsidering a balance between the scientific reliability of clinical trial results and the approved health claim. The important thing is to inform the consumers of the health effect based upon scientific facts. Therefore, an appropriate description should be prepared corresponding to its scientific facts.

In the future, we hope to obtain a government approval for the clearer labeling of beneficial health effects for humans in cases where scientifically evident intervene clinical trials have been performed. Also, appropriate guidelines, which are useful to establish scientific reliability for clinical trial results, are desired.

On the other hand, problems exist for manufacturers of FOSHU who bear a heavy burden financially for the cost of development. Secondly, there are ethical problems such as protection of human rights for the subjects, although clinical trials are the most important foundation to support the scientific ground for the health claim. If possible, alternative non-clinical tests or measurement methods are desired. The health claim is unlike that of medical drugs because its use is different from treatment or diagnosis of diseases. For example, clinical indices such as measurement of the reduction of tumor size, which is used to evaluate efficacy of an anti-tumor agent, are not necessary for functional food. The efficacy of functional food can be evaluated if it can suppress the development of the disease by referencing the physiological changes that may relate to the onset of the disease.

Based on this consideration, a concept to apply a "marker" is being proposed. In European countries, mainly at the European Branch Office of ILSI, the importance of "marker" was pointed out during the investigation of functional food. And a development of a new "marker" was taken as the major theme for future research and development of

functional food. In Japan, the "marker" is being studied for its importance as the indices for evaluation. However, the development of the "marker" has only recently started, and has not yet replaced the significance of the clinical trial results. In the development of "markers", which will be the indices for the condition of human health, a promotion of a systematic basic research is strongly desired. This would include absorption of constituents of ingested food, their metabolism, or internal kinetics, delivery/action to the target site of the body, and the methods to deal with the clinical trial and epidemiological research results. Because all of these basic research items cannot be performed in one company, collaborative work with researchers of various fields, including medical science, is necessary. Therefore, an arrangement of a national support system is desired in some areas.

(III) Proposal for the labeling of beneficial health effects

Many years have passed since an aging population and increasing medical care cost came to be regarded as social problems. In recent years, a concept of "life-style related disease" has been applied for adult diseases such as cancer, cardiovascular diseases, and cerebral stroke. This is due to the idea that the onset of such diseases can be prevented by improvement in one's life-style. It has been widely acknowledged that appropriate eating habits will play an important role in maintaining a healthy condition, prevention of diseases, and reducing relative risk of disease. Among information related to health care, labeling on food (so called functional food and nutritional supplement food) shares an important role.

Based on these circumstances, an introduction of the following descriptions regarding health-related claims is urged.

The most important thing in the labeling of food is that the consumers can correctly understand the features, contents, and usage of the food. Therefore, the labeling should be clear for the consumers and avoid any misunderstanding.

The term, *Health-Related Claims*, can be classified into the following three major categories: 1) *Nutrient Function Claim*, 2) *Structure/Function Claim* or *Enhanced Functional Claim*, and 3) *Health Claim*. The labeling of these foods should be made based on scientific evidence always bearing in mind harmonization with global international standards because the food business is being globalized. Active discussions are necessary in the Codex Committee on Nutrition and Foods for Special Dietary Use(CCNFS) and the Codex Committee on Food Labeling(CCFL) of the Codex, to reflect the opinions of Japan

and Asian countries, considering international harmonization of the systems, laws and regulations. In the labeling of functional food, supplemental conditions such as the adequate intake should be written in order to prevent new problems such as excessive intake. Beside the indications on the label, a campaign for general education is necessary through school programs and adult consumer re-education by the food industry.

1) *Nutrient Function Claim* : According to the definition approved by CCFL of the Codex in 1995, the *Nutrient Function Claim* should cover the growth of the body and physiological role of the nutrients. The nutrients include the 3 major nutrients, 10 different kinds of vitamins, and 6 different kinds of minerals. All of these are internationally approved as nutrients in general. An example of such a description is "calcium aids in the development of strong bones and teeth."

2) *Structure/Function Claim* : The *Structure/Function Claim* should describe that physiological action of nutrients or non-nutrients will provide good effects on the growth, healthy physiological structure, and function of the body. Nutrient was not defined to be included in the *Enhanced Functional Claim* proposed by CCFL of the Codex in 1999. However, nutrients excluded in the Codex were limited to the above mentioned nutrients only, and other nutrients are considered to be included in the *Enhanced Functional Claim*. The purpose of the *Structure/Function Claim* is the description of nutrients and non-nutrients excluded in the Codex. The contents should be similar expressions to those of the European Commission Concerted Action on Functional Food Science in Europe, which is co-ordinated by ILSI Europe.

For FOSHU, the labeling of constituents of the *Structure/Function Claim* has been approved to describe the components of food of which the scientific effect is proved. This includes conventional nutrients. The project of ISLI Europe also includes nutrients and non-nutrients as well as specified supplement food. It applied the *Enhanced Functional Claim* that is the same as that in the Codex. In 1994, the Dietary Supplement Food Education Act (DSHEA) of America enhanced description on the structure and function in vitamins, minerals, and herbs, along with their respective scientific evidences.

3) *Health Claim* : The health claims are to describe the positive effects of the nutrient or other substances in the food which provide improved strength in disease resistance and in physical condition. The description should be limited to the reduction of disease risk and improvement of health, however, it should not be applied to descriptions which may relate to the pharmacological efficacies such as prevention or treatment of diseases. For example,

a description, "risk of having osteoporosis can be reduced by the ingestion of calcium" belongs to the health claim category. But the description, "osteoporosis can be prevented by the ingestion of calcium" is currently not approved.

Most of the descriptions of Japanese FOSHU are close to the category of the *Enhanced Functional Claim*. Although their descriptions are approved to mention an improvement effect on a preliminary stage of a disease or a borderline condition due to an unbalanced nutrient state, a description which relates to the disease itself is not approved. In America, the Nutrition Label Education Act (NLEA) in 1990 approved mention of a specific disease name with FDA approval. Labeling regarding reduction of disease risk has been proposed in LSI Europe and the Codex. Further consideration is necessary to approve the labeling method of FOSHU with relation to specific diseases, along with so-called "dietary supplement food", which is presently under discussion.

(IV) Proposal for maximum use of labeling

1. Revision of the definitions in the Pharmaceutical Affairs Law, reconsideration of the 46 Notifications, and a new systemized differentiation between food and drugs

After revision of the Pharmaceutical Affairs Law in 1960 in Japan, Item 3 of Article 2 (Definition of pharmaceutical products) states: Medical drugs were defined as "the products desired to effect the physical structure or function of humans or animals, not including equipment or devices (excluding quasi drug and cosmetics)." Whereas, food was defined as food and drinks which do not fit the category of medical or quasi drugs.

The phrase "excluding food" had been written in the above definition before revision. This indicates that although things which effect physical structure or function were approved in some general foods, the revision stated the category of food was defined not to influence physical structure or function. In 1971, the standard for the category of pharmaceutical products was established in the 46-notifications. This stated that pharmaceutical products should be comprehensively decided according to the constituents' substantial substances, forms, labeled contents, and other information. It was stated that "obvious food" and "Foods for special dietary uses" defined in Article 12 of the Nutrient Improvement Act are not categorized as pharmaceutical products. We can interpret that the Pharmaceutical Affairs Law will not be applied to these two lines of products, even if

they are supplied in order to effect one's physical structure or function through ingestion.

Enactment of a new regulation is necessary, which repeats the old phrase "excluding food". It should clearly define that regarding food and drugs, "some foods have an effect on the physical structure or function of humans or animals", and supervise the industrial activities. In other words, reconsideration of the 46 Notifications and the alternative differentiation concept of food and drugs are necessary.

New government systems to comprehensively deal with the issues of food which directly relates to daily life and health of citizens are necessary in order to meet the medical cost reduction policy and to support aging populations with increasing consciousness of health maintenance. For this purpose, a new Japanese government system is desired to be restructured, that is, being combined food and drug categories and administers these similarly to the FDA, or being unified administration of production, safety, sanity and labeling of food which corresponds to the system "Directive General 12" of EU. However, in order to reform the Japanese government system for prioritizing medicine, the EU type management might be the better fit, because it has a strong specialized section with a unified administration system for food.

2. Approval of food additives related to nutrients

There are many food additives, which are approved in the USA and EU, but not approved in Japan, although regulations on dietary supplements such as vitamins and minerals are being eased. For example, in minerals, appropriate sources of supplies such as zinc and selenium are not approved and cannot be incorporated into food products practically. For international harmonization, a system is necessary to substantially consider the status of the approval in foreign countries and the actual results of eating habits. With respect to safety and approval, there should be some exceptional cases to incorporate food additives into products relying on the responsibility manufacturing companies, such as "GRAS" and "Self GRAS" in America. This would replace requiring the approval of the Minister of Health and Welfare for all food additives. Therefore, collaboration between the government and the industrial companies is necessary to discuss the establishment of an organization to evaluate safety and approve food additives.

3. System for labeling

An individual investigation committee of the Director General, Environmental Health Bureau, the Ministry of Health and Welfare in Japan, "Investigation Committee on handling so called dietary supplements" was established in December 1998. The committee has been investigating vitamins, minerals and other nutrients as a new category. In the official report issued by the investigation committee on June 16, 1998, it stated that "(dietary supplement) is a food packaged in the form of capsules or tablets. It is designed to supply vitamins minerals and other nutrients, which are lacking due to unbalanced eating habits. More scientific research is necessary in various aspects including education of consumers, definition of appropriate amounts, and appropriate labeling." Kinds of nutrients, shapes of food, appropriate labeling, and problems in management were considered in this investigation.

The first step was to define the kinds of the nutrients. Establishment of a labeling system is necessary regarding the functions of 16 vitamins and minerals. These are mentioned as the subjects for the *Nutrient Function Claim*, which was approved by the Codex in 1995. Secondly, nutrients considered to be deficient in Japanese people need to be added, as mentioned in the 6th edition Recommended Dietary Allowances and Dietary Reference Intakes in Japan.

Regarding the labeling and administration of this system, comparative study with the existing FOSHU is necessary. The nutrients for this investigation should be the ones defined according to various health benefits. Standard intake and upper limits for safe ingestion as well as function should all be based on solid scientific facts. Using this premise, individual verification of each functional product is not necessary. However, a fixed and common standard should be established for labeling each nutrient for proper management.

The form or shape of products need not be regulated, since nutrients are better ingested as ordinary forms of food than forms of capsules or tablets. Therefore, ordinary forms of food should not be excluded in the regulation to avoid excessive ingestion to supply nutrients to cover the tendency of alimentary deficiency. That is, considering the first priority is to maintain health of citizens.

Regarding the claims, we suggest that the government at first should propose a rule on the specific labeling description and then opinions should be received from the general public.

In the legalization of the *Structure/Functional Claim* and *Health Claim*, a harmonization with the existing FOSHU, which currently has a part of the labeled items, is necessary. Dietary supplement is defined for scientifically proven food constituents. However, verification for the function of these two health claim items is not sufficient in

general. Therefore, it is necessary to examine each subject food. From this viewpoint, a product-specific study is considered appropriate. It would be similar to that for FOSHU. Regarding these two *Claims*, we consider that an investigation on the extended understanding of FOSHU system would be appropriate for international standardization and prompt action.

In the expanded application of the labeling contents, the reduction of the risk of diseases is the issue. The labeling description for the risk reduction of diseases has been discussed on the point that the differentiating it from the "prevention of diseases" is not clear. Specialists have also been investigating the decision not only in Japan but overseas. In the future, the term that clearly differentiates from the meaning of "prevention" should be defined by the collaboration between the industrial companies and the government. This would familiarize the new term in the same way the term "life-style related diseases" is getting to be generally understood as replacing the term "adult diseases".

The classification of *Function Claim* on food and regulatory established food is defined as follows:

Table 1. Classification of FOSHU and "Dietary supplement"

	Standard Regulation Type (Generic function labeling)	Individual Inspection Type (Innovative function labeling)
Nutrient Function Claim	"Dietary supplement"	FOSHU (existing)
Structure/Function Claim (non-nutrient)	Not exist currently	FOSHU (existing)
Health Claim (Risk reduction of diseases)	Not exist currently	FOSHU (not exist currently)

4. Systemization of prioritization of developers

Foods in general that exist in the natural world commonly and have been eating for a long time are difficult for material patents. Industrial proprietary rights cannot be sufficiently covered by a patent only because similar substances may follow which are manufactured from other types of edible raw materials, even if an approval for labeling is obtained after discovering a new physiological function in the constituent of food and confirmation of safety. Although a long-term monopoly should not be held by the company which developed the product, a certain prioritization is desired for that company. The idea is the company, which obtained the scientific data individually confirms the safety, develops the constituents and materials which have a new function, and launch the production. Then, a regulation for a certain period is to be allowed for the company, which developed the product that prevents other companies from developing similar functional products using similar material. Such a system will be an incentive for a company to develop new products with health benefits, and will promote research and development hopefully.

(V) Education of consumers and responsibility of industrial companies

Anxiety regarding health is increasing among Japanese people centering on life-style related diseases due to current westernized eating habits, increased mental stress, and lack of physical exercise (according to the "Survey of people's consciousness on life-style related diseases" of the Tokyo Metropolitan Bureau of Public Health.) Since the influence of eating habits on life-style related diseases is significant, suppression and prevention of the onset of the diseases will be possible by making changes in dietary patterns. A complicating factor is that most of the life-style related diseases are chronic, and patients are often not so much aware of their subjective symptoms. Also, mild-stage patients tend to want to manage themselves without using pharmacological agents. Therefore, many people desire food that will help maintain health, prevent life-style related diseases, and subdue the advancement of symptoms.

Since long ago, so-called "health food" has been sold in Japanese market. However, the quality of most such "health food" did not fulfill the requirement of "health food" for consumers. This is because the accurate labeling of its function is not possible due to strict restrictions on health effect labeling by the Pharmaceutical Affairs Law of the Japanese government.

Information on health food materials has been disseminated through media, such as

TV, newspapers, and journals. However, information based on scientific grounds, universality, safety, and relation to medical drugs is not sufficiently given. Therefore, consumers have been confused with the information they see and hear. In the future, it is necessary to provide needed information from a collaboration of government, companies and researchers, which is based on the current nutritional and health condition of people.

Companies should introduce appropriate and scientifically proven products to consumers. For this purpose, special sales staff, who know comprehensive information on the scientific ground of the labeling and standard regulations, are necessary to provide information and introduce the most appropriate products for consumers. On the other hand, consumers select the optimum product for their own health condition based on the information they receive. Both the companies and consumers should be aware of the responsibility for the selection and action they make by themselves. To achieve these purposes, we propose to establish the following facilities and systems in the future:

(1) Establishment of an institute to provide information on food

We propose to establish an institute with collaboration of industries, government, and academic organization to provide comprehensive and current information from domestic and international sources. This would be regarding the following food-related items that influence health based on confirmation by scientific facts.

- ① Physical condition adjustment function.
 - Effectiveness and function confirmed by evaluation tests.
 - Mechanism of active function
- ② Appropriate oral dose.
- ③ Problems of an overdose or ingestion by inappropriate persons
- ④ Domestic and international experiences of eating.
- ⑤ Forms, and contents, specification, standard and delivery route of the product.
- ⑥ Discussion content on food for individual evaluation between companies and the Ministry of Health and Welfare of Japan.

(2) Establishment of official qualifications

Provide training to have specialists with official qualifications in basic biochemistry, nutrition science, food hygienics, and domestic and international food-related laws and

regulations. These specialists would all possess a knowledge level equal or greater than that of a dietitian. Such specialists are necessary in sales to provide consumers with information based on scientific evidence and to introduce commercial products which will suite each consumer. In the future, a rule will be necessary to have staff with special qualifications in each shop; for example, a pharmacy should have a pharmacist.

§ 3. Contents of Investigation

(I) Laws and Regulations

1. Domestic Laws

1.1 Pharmaceutical Affairs Law

According to the pharmaceutical affairs law of Japan (for drugs and quasi-drugs), three categories are allowed to be mentioned as nutritional supplements, i.e. vitamin-containing health preparations, vitamin-base preparations, and calcium preparation. Although all of these are prepared using vitamins and calcium as their main constituents, the possible combination and the expected efficacy are different in each preparation. The contents are explained as follows:

1.1.1 Vitamin-containing health preparation

Vitamin-containing health preparation is defined in the guidelines of drug manufacturing as follows: "it is a health preparation which is a compound of general vitamins and vitamins combined with amino acid, drugs for liver disorder, herb medicines, or organ extract preparations. In general, it is a compound with either vitamin B1, B2, or B6."

Vitamin tonics, mini-vitamin tonics, and general vitamin preparations, which have the largest market share among general drugs, are considered to be included in this category. Table 2 shows the possible compound and amount of each vitamin and minimum and maximum daily dose. The conditions of herb medicines, excluding vitamins, are expected to fit under the regulations of the previous approvals, and the only way to investigate the product is to check each company's product.

Table 2. Daily dose of vitamins for vitamin-containing health Preparations and for general vitamin preparation. (Oral dose for one adult person)

Vitamin name	Maximum dose per day	Minimum dose per day	Notes
Vitamin A	2,000 IU	500 IU	As vitamin A
Vitamin D	200 IU	50 IU	As vitamin D
Vitamin E	100 mg	10 mg	
Vitamin B	1.25 mg	1 mg	
Vitamin B2	12 mg	2 mg	
Vitamin B6	50 mg	5 mg	
Vitamin B12	60 μ g	1 μ g	
Vitamin C	500 mg	50 mg	

Note: Please refer to the approved standard for the vitamin-base preparation manufacturing regulation regarding the contents of the constituents in each drug.

Label Claims indicating effectiveness on health are allowed as follows:

[Efficacy and Effectiveness]

This is for nourishment and sthenia, infirmity, physical fatigue, and reduced physical strength during and after illness. It also works for gastrointestinal disorder, malnutrition, wear and tear from high fever, nutrition supply during pregnancy or lactation period (before and after delivery).

Vitamin-containing preparations are made for various purposes including times of weakness and loss of appetite during or after illness, fatigue after exercise or heavy physical work. They also serve as a nutrition supplement during pregnancy or the lactation period. However, the labeled efficacy and effectiveness for such vitamin-containing drugs are all similar irrespective of the different combination of ingredients. This is a direct result of the notification "Regulation on self-imposed evaluation and check-ups regarding the effectiveness of vitamin-containing health drugs", which was issued by the Pharmaceutical Affairs Bureau, Ministry of Health and Welfare of Japan. The purpose of the notification was to unify various applications regarding efficacy and effectiveness of various health drugs from each manufacturer.

1.1.2 Preparation of vitamin-base components

This category applies to oral doses of vitamin preparations made with one or more vitamins as the base. These are adjusted in order to reduce clinical symptoms and supply vitamins, increasing the effectiveness of vitamins.

In other words, vitamin-base preparations to treat specific clinical symptoms are considered to fit into this category. They are classified into 11 kinds of vitamins according to the effective part of their main constituents; i.e., vitamin A, D, E, B1, B2, B6, C, A-D, B2-B6, E-C, B1-B6-B12. Possible compounds other than vitamins such as herb medicines or natural remedies are also regulated in terms of kinds and dosages.

The descriptions for efficacies and effectiveness allowed to be labeled are limited as follows:

- (1) Reduction of the following symptoms:
- (2) Supplement of vitamin XX for the following cases:

1.1.3 Calcium preparations

Calcium preparations are made to supply minerals.

This category drug is prepared with a calcium compound such as calcium lactate or calcium gluconate. The efficacy of calcium preparations are as a calcium supplement for infirmity, promotion of development of bones and teeth in case of scrofulousness, and prevention of bone and tooth degeneration for pregnant or breast-feeding women. This would also be used during the pregnancy and lactation period, growing period for children, and aged people.

There have been no general drugs allowed to label efficacy and effectiveness for supplying minerals other than calcium. As part of the above mentioned

vitamin-containing health preparations, calcium preparations, and vitamin-base preparations are being investigated to be categorized as a quasi drug after a new government policy relaxing official restrictions.

1.2 The Nutrition Improvement Act for FOSHU and Food for Patients

1.2.1 FOSHU

In Japan and other developed countries, it used to be completely forbidden to mention on the label information regarding the effects of food on health. People question why it was not allowed to provide the public with information how a diet interacts with health, considering health is maintained by food until the end of life. In the US, the Food and Drug Administration (FDA) used to implement stringent regulations in terms of health-related labels on food, however, they softened their policy in the end of 1980's so as not to increase the number of geriatric diseases and medical expenses. And they approved the Nutrition Label Education Act (NLEA) in 1990, in which a *Health Claim* can describe the relationship between nutrients and their effect on preventing specific diseases.

Japan had started talking and has taken the lead in the world by offering a proposal concerning the function of food in accordance with particular research of the Ministry of Education. This was called "the Systematic Analysis and Development of Food Function" from 1984 through 1986, which was before the FDA took action on the said matter. This research identified three functions of food, which is nutrition as the primary function, sensory satisfaction as the secondary function, and modulating the living body conditions as the tertiary function. Then, a food, for which the tertiary function is recognized, was defined as a functional food. Almost simultaneously in the market, we began to see products that advertised an effect by the tertiary function and gradually sold as a functional food. The market had already been flooded with so called, "Health Food" whose precise scientific evidence had not been proved. This caused discussion among industries, government, and the academic world suggesting necessity of a law or regulation to label health information provable by scientific evidence. The investigation at that time reported side effects from health food due to excessive ingestion. This is considered one of the reasons why a health food label was not allowed to describe methods of use or dosages.

Under these circumstances, the Ministry of Health and Welfare organized "the Functional Food Discussion Session" in 1988. In their interim report on "Discussion Results of the Issuers of Functional Food", the following was written: "While the expanded average life span is turning the world into an rapidly aging society, the majority of diseases changed their features from infectious diseases including acute infectious disease to chronic diseases including geriatric diseases. Regarding life-style related diseases, it has been widely recognized that the first line of defense against disease is an improvement of one's diet. It is desirable that consumers choose the appropriate functional food depending on their personal needs. In order to make this happen, a label with customer-friendly and useful information is necessary, especially regarding the function of food based on scientific evidence."

In March 1990, the Office of Health Policy on Newly Developed Foods in the Ministry of Health and Welfare established "the Functional Food Study Committee" and went into detail to prepare the standard for functional food. In November of the same year, this committee submitted a report entitled, "The proposal for legalization of functional food". In the July, 1991 issue of the Official Gazette, a *ministerial ordinance* was given stating "Partial modification of the regulations of the Nutrition Improvement Act". The Director-General of the Environmental Health Bureau announced the notification regarding enforcement of this law. Owing to this action, in September 1991, "FOSHU Labeling Approval System" was enforced in Japan. This preceded other countries, which still allowed label information on the physiological control function of food. Although the name, functional food was replaced by a new name, FOSHU, it still holds the aim of maintaining or improving health through diet. This includes improvement in the condition of people who may be potential patients or at risk for getting life-style-related diseases due to an unbalanced nutritional state. According to this law, labeling of health related information was allowed for the food products after obtaining approval from the Ministry of Health and Welfare, but only in cases where the contents of the food are proven to have effective benefit to health proven by scientific data. Then, the FOSHU was defined as a food, which is expected to show efficacy on health making it possible to label the food function and usage. The first approval of labeling was enforced in 1993. Then, in October 1997, after six years had passed since this approval system began, the Ministry revised "the Guidelines for FOSHU Food Approval" and the related items. This was after confirming the system had been relatively well-obeyed in the past years. As a result, the application procedures were substantially simplified, and they abolished the expiration date of approval, which had been limited to four years after approval.

There have been changes in application items after the simplification of the labeling approval system. Twenty-seven new products were added to FOSHU as of July 23, 1999, which increased the total to 153 items. Among these items, one product was approved to show two categories of health benefits. After almost a year had passed since the revision of contents of the labeling approval system, guidelines for application and evaluation of FOSHU were released for two categories among the "effective constituents". These were food "to control digestion" using oligosaccharide and food "to reduce incidences of decayed teeth" using alternative synthetic sweetener.

1.2.2 Food for Patients

Patient food is categorized as "Food for Special Dietary Use" in Article 12 of the Nutrition Improvement Act. Supplement food also belongs in the same category. It stated "those who intend to label information on food for sale, i.e., descriptions to supply nutrition or to claim usefulness for special cases, such as for babies, infants, pregnant women, or patients, should receive approval from the Ministry of Health and Welfare." In the beginning, the foods approved by article 12 were called Special Nutrition Food. Since then the need for patient food has been growing due to the increase of chronic diseases, such as diabetes and hypertension, derived from an enriched diet.

Under the circumstances, considering the report from the Council of Public Health

(Sub-Committee of Health Improvement) held on April 13, 1998, a partial revision of the Notification of Director-General, Environmental Health Bureau was announced. This was regarding "Approval of the Labeling of Special Purpose Food." There had been approval criteria of single foods such as a low sodium diet or formulated foods such as a diabetic diet. The main purpose of this notification revision was because an individual evaluation regarding an approval standard for food labeling had not been prepared for each food group. It stated new approval requirements for labeling as foods for patient and a new definition of alimentotherapy. The major requirements in the revision were as follows: the food should achieve the purpose of alimentotherapy for a particular disease, have good prospects for the improvement of dietary life, have a proven effect as a diet therapy based on medical and nutrition science, edible as a ordinary food, and have an ordinary form of food. For an individual evaluation of patient food, the Study Committee was comprised of academic specialists nominated by the director-general of the Environmental Health Bureau of the Ministry of Health and Welfare. They were supposed to be asked comments prior to decision-making as to whether the food was appropriate as patient food.

The meaning of alimentotherapy here is defined as follows: "A prescription by a medical doctor to a patient, regarding food for treatment of a disease or for prevention of disease recurrence, based on knowledge from medical and nutrition sciences. It was reported that in April the Council of Public Health started a heated discussion about who plays the leading role in alimentotherapy, a doctor, a dietitian or a patient. In the Director-General's notification "the Approval Standard in Each Food Group," it stated "The food should be used after counseling and instruction given by a doctor or an administrative dietitian." This is one of the necessary labeling items for a single patient food. Whereas, the description for a combination of patient food stated that "the food should be used with detailed instruction from a doctor or administrative dietitian on the menu of food." The Ministry of Health and Welfare fully considered the situation from both domestic and international viewpoints before making this partial revision. Two categories were announced to classify patient food as a special purpose food according to the new approval method: the standard approval type and the individual evaluation type.

1.3 Reconsideration of the differentiation between food and drugs

1.3.1 The reasons for differentiation between food and drugs

A differentiation between food and drug was stated in the Notification of Pharmaceutical Bureau of the Ministry of Health and Welfare, which is generally referred to as the 46 Notifications. IT IS titled "Instruction and regulations on unapproved medicine." In "the standard of the category of medicine," it is stated that " ... will be judged by comprehensive considerations including the constituents, characteristics, features (such as the form of the drug, container, package, and design), and labeled items. these include purpose of use, efficacy and effectiveness, administration method, dosage, methods for sales, and demonstration on sale."

As factors in judging whether something is suitable as a drug or not, the following 4 items are used:

- (1) Category based on the substantial components.
- (2) Interpretation of pharmacological effectiveness.
- (3) Interpretation of the shape of the would-be drug.
- (4) Interpretation of the medical administration method and dosage.

Among above-mentioned items, the (1) Category based on the substantial components and (3) Interpretation of the shape of the would-be drug are considered the most important points in the re-consideration of the differentiation between food and drugs.

1.3.2 Classification between drug and food. Relationship between categories based on the substantial components, pharmaceutical efficacy, the shape of the would-be drug, the administration method and dosage.

(1) Substantial components used in the would-be drug.

a. Substantial components primarily used as a drug [1-a Constituents]

If the 1-a Constituents are used as a compound or component, the substances is regarded as a drug, no matter what kind of its effect, administration method, or dosage.

b. Substantial components mainly used as a drug [1-b constituents]

- ① The label indicates pharmaceutical efficacy.
- ② The shape, administration method, and application are considered for the would-be drug.

If the shape is obviously considered as that of a would-be drug, then the material is regarded as a drug, no matter what kind of its administration method and dosage.

c. Materials which may be used as food an ordinary dietary life [1-c Constituents]

- ① The label indicates pharmaceutical efficacy.
- ② The shape, administration method, and dosage are considered as that of a would-be drug.

If the shape is obviously considered as that of a would-be drug, then the material is regarded as a drug, no matter what kind of its administration method and dosage. However, some materials may not be regarded to fit this category, even though their shape is a tablet, pill, or capsule. This exception applies to materials which may be objectively recognized by shape as an oral dosage in order to assure quality, and the design and form of the container or package may not impress one as a drug.

- (2) Substantial components of which the constituents have been used in accordance with customs and traditions, also have an expectation to show efficacy as the would-be drug.

a. Materials which cannot be recognized to be within the category of food in an ordinary dietary life [2-a Constituents]

- ① The label indicates pharmaceutical efficacy.
- ② The shape, administration method, and dosage are considered as would-be drug.

If the shape is obviously considered a would-be drug, then the material is regarded as a drug, no matter what kind of its administration method, and dosage.

b. Materials which may be used as food in an ordinary dietary life [2-b Constituents]

- ① The label indicates pharmaceutical efficacy.
- ② The shape, administration method, and dosage are considered as would-be drug.

If the shape is obviously considered a would-be drug, then the material is regarded as a drug, no matter what kind of its administration method and dosage. However, some materials may fit this category, even though their shape is a tablet, pill, or capsule. This exception applies for materials which may be objectively recognized to be the shape for an oral dosage in order to assure quality, but the design and form of the container or package may not give the impression of a drug.

*Some vitamins and minerals are included among the exceptional constituents, which are categorized as the above mentioned 1-b Constituents.

1.3.3 Relaxation of the regulations

The following guidelines are given by the Ministry of Health and Welfare to reduce regulations.

(1) Guidelines for vitamins

In the March 31, 1997, Notification from the Director-General, Pharmaceutical Bureau of the Ministry of Health and Welfare, the regulation on 1-b. category (regulated constituents by form such as a capsule and a tablet) was exempted for 7 constituents. These included vitamin A, vitamin B1, vitamin B2, vitamin C, vitamin D, vitamin E, and niacin. The regulation can be applied to those which are labeled as food but are not labeled to indicate efficacy. (Other vitamins are to follow the regulation as before.)

(2) Guidelines for herbs

In the Notification issued March 31, 1998, the regulation on forms such as a capsule and a tablet was exempted for 7 herbs. These 7 herbs are Acanthopanax and leave of Ginkgo biloba of the 1-b Constituent, in addition to the newly added Echinocea, Serenoa serrulata, Silybum marianum, Hypericum perforatum, Oenothera biennis of the 2-a Constituents.

Some of the herbs, which were not included in the relaxation of the regulation at

that time, have been investigated and discussed, due to many requests from foreign countries to reduce the regulation.

(3) Guidelines for minerals

The following Notification of the Director-General was announced March 31, 1999 through the work of the Investigation Committee:

The regulation on the forms, such as a capsule and tablet, was removed on calcium, iron, magnesium, phosphorus, and potassium. Also, if it is within the limit of the dosage, chromium (III), selenium, copper, fluorine, molybdenum, and iodine were approved to remove the regulation. The condition of these items is as long as a word "food" is used in the label and an efficacy is not indicated on the label.

The Ministry of Health and Welfare commented that they would try to consider each herb, but only following discussion after they obtain safety data. However they are not scheduled to revise the general concept of 1-a Constituent (sectional revision) which food industries have been eagerly requesting.

1.4 Legal System for so-called "Dietary Supplements"

1.4.1 The meaning of so called "dietary supplement"

Although the word "dietary supplement" has been generally used, the word has not been officially defined. The meaning of dietary supplement is generally considered as "food to supply nutrients". In the Japanese market, dietary supplements are classified into two major categories: 1) Food which can provide balanced nutrients and 2) Food which can provide specified nutrients

1.4.2 Trend in legal aspects of "dietary supplements"

There have been no administrative regulations on the word "dietary supplements" in Japan. However, the trend in the relaxation of the regulation was that the food and drug differentiation in the so-called 46 Notifications and the category of 7 kinds of vitamins which are typical constituents of "dietary supplement" was changed from "drug" to "food".

Owing to these changes, vitamin compounds, such as tablets and capsules, which have pharmaceutical forms, were categorized as "food". Therefore, the vitamin supplement market was activated.

However, the definition of pharmaceutical agents "applied for diagnosis, treatment, or prevention of human or animal diseases" still remains in the Pharmaceutical Affairs Law in Japan. Thus, efficacy for vitamin supplements cannot be claimed. For example, the expression "Prevention and treatment of vitamin C deficiency" can be used for drugs only, and in case of dietary supplements, an expression mentioning "food" is necessary and the claim limited to only "maintaining health" or "for improvement of health". These days certain reduction of regulations was given for minerals [please refer to the previous section (1.3) Reconsideration of food and drug differentiation.]

In the June 1998 report of the Food Sanitation Investigation Committee of the Ministry of Health and Welfare, sentences regarding "The measures for dietary supplements" were written in their report of "Policies of the administration for food in the future". It suggested a positive meaning by saying "dietary supplements such as vitamins and minerals will become an aid to promote health in dietary life in the future." This report also stated that study on appropriate labeling is necessary for effective use of dietary supplements.

Meetings by the "Investigation Committee of handling "Dietary Supplements"" were held 3 times from April 1999, to discuss categories, forms, contents of labels, and inspection methods of substances included in dietary supplements. The Ministry of Health and Welfare was scheduled to make an interim report by December 1999 and draw up a plan by February 2000.

In relation to labeling for appropriate ingestion, "The 6th revision of Recommendation Dietary Allowances and Dietary Reference Intakes for Japanese people" was officially announced in July 1999. Guidelines on the kinds of nutrients and the amount of ingestion which had not been mentioned in the previous revision were written in the 6th revision. . It included not only vitamins and minerals as defined in the Codex of 1995, but also other nutrients. In September 1999, an official document was published which included an explanation of the functional and scientific grounds for these guidelines.

1.4.3 Differentiation from foreign laws and regulations

After dietary supplements are considered as food, the opportunity for importing foreign products will increase. However, some problems regarding foreign trade have been raised, because some foreign products contain constituents such as biotin and tocopherol acetate that are not approved in Japan as "food additives". For example, melatonin has been sold as a dietary supplement in the USA, but has been categorized as a drug in Japan. The Ministry of Health and Welfare clearly stated that production, sales, or import of melatonin cannot be approved as food in Japan.

2. Foreign Laws and Regulations

2.1 CODEX

2.1.1 Discussion Items at the 25th CODEX Meeting

The discussion on *HEALTH CLAIMS* in the CODEX started at the "Investigation on the draft of guidelines regarding Health and Nutrition Function Claim" of Codex Committee on Food Labeling. At the 24th Meeting in May 1996, the *Nutrition Function Claim* was chosen to be independently discussed and then was adopted as the topic preceding other Claims.

In the 25th Meeting in April 1997, the conclusion was made regarding *HEALTH CLAIMS* to restart on Step 3, which is the "Stage to request comments after distributing draft regulations prepared by the Secretariat to each foreign government and international organization." The main ideas in the Meeting were as follows:

2.1.2 Discussion Items at the 26th CODEX Meeting

Although active discussion was made at the 26th Meeting in May 1998, not all agreements were obtained for each discussion item. Therefore, the exchange of opinion for each country was continued based on the step 3 stage. Also, it was decided to seek advice at the Nutrients/Specified Purpose Food Meeting, which was scheduled to be held in September 1998 in Berlin.

2.1.3. Discussion Items at the 27th CODEX Health Claim Meeting

At the 27th Health Claim Standardization Committee in Ottawa in April 1999, the USA and Canada proposed further discussions by the working group. And the UK and France agreed to cooperate. This was to be followed by a discussion of the working group during the meeting period.

After those discussions, the revised draft for *Health Claims* was made during the meeting period. At the next meeting in 2000, comments from each country are going to be summarized as the Step 3 stage of the meeting. At present, the draft is being prepared, and the definition is proposed as follows:

(1) Health claims means any claim establishing a regulation between a food or a constituent of that food and health, [whether it is good health or a condition related to health (or disease)].

Or,

(2) Health claims means any claims which suggests that a food or a constituent of that food has an impact on health.

(a) Enhanced Function Claims:

These claims concern specific beneficial effects of the consumption of foods and their

constituents on physiological, [or psychological], functions or biological activities but do not include nutrient function claim. Such claims relate to a positive contribution to health or to a condition linked to health or to the improvement of a function or to modifying or preserving health.

(b) Reduction of Disease Risk Claims:

An ordinary healthy diet will reduce risks of specific diseases or conditions. This means a label showing the relationship between ingestion of the food or the constituents of food and reduction of risk of disease.

Risk reduction means significantly altering a major risk factors, or factors recognized to be involved in the development of a chronic disease or adverse health-related condition. Helping to reduce risk does not constitute "prevention" as is meant in the General Guidelines on Claims.

2.2 North America

2.2.1 Regulation in the United States (NLEA, ADSHEA, 98/4/29FR, AFDAMA)

(1) The Nutrition Labeling and Education Act (NLEA)

In the USA, *Structure/Function Claim* and *Health Claim* are defined for food by two laws. The first law is the Nutrition Labeling and Education Act (NLEA) that was established in 1990. It allows food to claim that some nutrients may prevent specific diseases in cases where the scientific causality between the nutrient and disease or health condition is acknowledged by the Food and Drug Administration (FDA). At the time of legalization, the following 8 items ① through ⑧ were approved, and later 3 items ⑨ through ⑪ were added:

- ① Calcium and osteoporosis
- ② Sodium and hypertension
- ③ Dietary lipids and cancer
- ④ Saturated fat and cholesterol and risk of coronary heart disease
- ⑤ Fiber-containing Grain, fruits and vegetables and risk of cancer
- ⑥ Grain, fruits and vegetables products that contain fiber, particularly soluble fiber, and risk of coronary heart disease
- ⑦ Fruits and vegetables (containing one or more of vitamin A, C and dietary fiber) and risk of cancer
- ⑧ Folate and neural tube defects
- ⑨ Soluble fiber from oats or psyllium and risk of coronary heart disease
- ⑩ Dietary Sugar alcohols contained in chewing gum and dental caries
- ⑪ Soybean protein and cardiac disease

According to an FDA report, there are some tens of foods which state the above mentioned health-related claims on the label according to the NLEA. (Source: R. S. Applebaum, "Labeling and Nutrition Policy Issue", Manufacturing Confectioner, Oct. 1997,

31-39).

(2) The Dietary Supplement Health and Education Act (DSHEA)

The second law is the Dietary Supplement Health and Education Act (DSHEA) which was established in 1994. It allows vitamins, minerals and herbs to indicate specific effects (i.e., effect on the structure and function of the human body) by simply giving the FDA notice as long as there is scientific evidence. There have been international debates regarding how food and drugs could be discriminated against as well as the differences between labels of action / effect for food and drugs.

(3) 98/4/29 Federal Register

In April 1998, the FDA proposed detailed regulations for claims describing effects on the structure or function of the human body (Structure/Function Claim), and now it is discussed:

In accordance with the FDA's survey, the total number of dietary supplements comes to 29,000 items, with labels for 75,000 items. The FDA received about 2,300 notices regarding structure/functional claims, and rejected about 150 of them. Sixty notices were rejected a second time. (Federal Register 63 FR23623 April 29, 1998)

(4) The Food and Drug Administration Modernization Act (FDAMA) 1997

Without the FDA's official approval this law enabled companies to make health claims. These claims were based on the documents published by the following designated federal institutions of science federal institutions of science. The condition for making a claim is that agreement is necessary through a consensus of an entire organization instead of an individual or a single division of a federal institution.

- ① The National Academy of Science (NAS)
- ② The National Institutes of Health (NIH)
- ③ The Centers for Disease Control and Prevention (CDC)
- ④ The Surgeon General from the Department of Health and Human Services
- ⑤ The Food and Nutrition Service, The Food Safety and Inspection Service, The Agricultural Research Service within Department of Agriculture

The prepared guidelines require an applicant to submit a document from the designated federal institution of science that describes the causality between nutrients and disease or health. Additionally the scientific evidence and reference literature should be attached. In case where the FDA acknowledges the application for labeling (Health Claims) and considers it inappropriate, the applicant will be notified within 120 days to make corrections. However, the product concerned is not allowed to be sold until the application process is completed.

2.2.2 Regulation in Canada

In November 1998, Health Canada, published a policy paper titled "Nutraceutical / Functional Foods and Health Claims on Foods." According to this policy, two projects have been organized. First is a project to legalize the labeling of standard type claims after reviewing the scientific evidence for 10 health claims approved by the NLEA of the USA. The other is the project to investigate the system that conducts a product-specific individual examination for newly applied health claims. The former project is going to reach a conclusion soon, however, the latter is considered a long-term investigation.

In Canada, American foods which make a health claim are allowed to be imported for personal use. This has caused a contradiction in that people can freely purchase this food with health claims at duty-free stores on the border or by mail order even though they are not allowed to sell or distribute within Canada. The Canada Health Food Association, an industrial group, is conducting a campaign including lobbying in order to resolve this contradiction.

In January 1999, on the other hand, the Canadian Functional Food Network was organized in collaboration with scholars from colleges and national institutes including the University of Guelph, federal/local administrative organizations and related business enterprises. Their mission was to conduct research and development of functional food, analyze market development, collect scientific evidence, and to provide information through the internet.

2.3 EU

There has been no Directive from the EU regarding guidelines for labeling concerning health-beneficial effects. The circumstances for labeling health-beneficial effects are different in each country.

2.3.1 ILSI Europe

The European Commission Concentrated Action on Functional Foods Science in Europe, which is co-ordinated by ILSI Europe, aims to establish a science-based approach for concepts in functional foods science. The goal of this Concerted Action has been to set up a multidisciplinary European network:

- (1) to assess critically the science base required to provide evidence that specific nutrients and food components positively affect target functions in the body.
- (2) to examine the available science from a function-driven perspective rather than a product-driven one.
- (3) to reach consensus on targeted modification of food and food constituents, and opinions for their application.

The contents of the first general assembly in April 1996 was published as

"Functional Food Science in Europe: State of the Art." The 3rd general assembly of November 1998 was published as "Scientific Concepts of Functional Food Science in Europe: Consensus Document." (Brit J Nutrition, 81 (suppl. 1), 1999).

In these projects, the selection of reference literature and the discussion focused primarily on the relationship between constituents of foods and the physiological function, along with markers to prove such relationships. They concluded that labeling of health-related items would be possible by selecting appropriate markers and proving the function of the food and constituents of food on the human body. This is proved by scientific evidences and substantiates evaluation data of the function by the markers. The following two kinds of labeling were mentioned:

Type A: Enhanced Function Claim

These claims concern specific beneficial effects of nutrients and non-nutrients on physiological, psychological functions or biological activities beyond their established role, in growth, development and other normal functions of the body. This type of claim is also similar to a "structure/function" claim in the U.S.A. For example, descriptions in this category are "Caffeine can improve cognitive performance" and "Folate can help reduce plasma homocystine levels."

Type B: Reduction of Disease Risk

These claims relate to the consumption of a food or food component that might help reduce the risk of a specific disease or condition because of specific nutrients and non-nutrients contain within it. These claims correspond to those referred to as "health claims" in the USA. For example, descriptions include "Folate can reduce a woman's risk of having a child with neural tube defects" and "Sufficient calcium intake may help to reduce the risk of osteoporosis can,

The difference between the two labeling categories is based on the selection of markers and their effects. There have been three kinds of markers: 1) Markers of exposure to food component, 2) Markers of target function/biological, and 3) Markers of intermediate endpoint.

2.3.2 U.K.

The Joint Health Claims Initiative was established in June 1997 and included a consumers' group, government organizations, and industrial society representatives. Its objective was to establish the *Code of Practice* on health claims on foods in the UK. The contents of its report, "The Final Draft for Consultation: Code of Practice on Health Claims on Foods", are summarized as follows:

The present legal and enforcement frame work governing claims is both incomplete and inflexible. There is a need to clarify and strengthen the requirements for evidence to substantiate health claims. Once scientific validity has been established, claims should be

able to express clearly and more directly the increasing variety of relationships between foods or food components and human health now being documented by research. There is a need for the government to review the existing law on food claims in the light of scientific advances, in particular the prohibition on foods claiming to prevent treat or cure disease can inhibit communication of the role of a healthy diet in maintaining good health and reducing the risk of disease.

Regarding the standards, generic health claims and innovative health claims were proposed to increase the possibility of coping with new developments in scientific research. It is claimed that labeling for disease risk reduction will be possible in some cases. "General Health Claim" means labeling based on well-established, generally accepted knowledge from scientific evidence. The Code Administration Body is responsible for developing a list of generic health claims for approval by the Expert Authority. In the case of generic health claims, no specific substantiation is required. On the other hand, For "Innovative Health Claim", a health claim other than a generic health claim, substantiation, or scientific evaluation is essential. Companies must show that the health claim is likely to be true and that the scientific evidence. The health claim must be based on a systematic review, that is, the totality of the evidence and human studies or evidence.

2.3.3 Sweden

Sweden preceded other countries by defining rules for the use of health claims in the labeling and marketing foodstuffs by an industrial self-regulating programme. The Food Industry's Rules; Self-Regulating Programme, was announced and implemented in 1990, and revised in 1996.

The rules are applied to foods, drinks, stimulants, and other products humans ingest except medicinal products. Medicinal products mean products for prevention, diagnosis, improvement, and treatment of disease or symptoms of the disease. Pharmaceutical Affairs Laws are applied to products of which the form is similar to medicine such as tablets and capsules, even when the raw materials of the product are made from general foods. However, the Pharmaceutical Affairs Laws are not applied in cases where the appropriate ingestion amount and medicinal information are not labeled on the products similar to general foods which could be set on a dining table.

The following claims are included:

(1) Health Claim:

1. The claim that the nutritional composition of the product can be connected composition with prophylactic effects or the reduced risk of a diet-related disease.
2. The health claim must be based on the importance of the product in a balanced diet, and must be in line with official Swedish dietary recommendation.
3. The claim must consist of two parts: information on diet-health relationships, followed by information on the composition of the product. An example is as follows:
Saturated fatty acids increase the level of cholesterol in the blood.
The product X contains low level of saturated fat and total fat.

(2) Nutrients Claim:

It contains information on the nutritional value of the product with no further connection to positive health effects.

(3) Nutrient Function Claim:

It means that the nutrition claim is connected to a generally accepted nutritional-physiological function.

(4) Foodstuff Intended for particular Nutritional Uses:

This category means foods approved by the National Food Administration in terms of application for 1) healthy infants, 2) individuals whose digestion or metabolism is impaired, and 3) individuals who can gain from controlled intake of certain compounds due to special physiological conditions.

(5) Natural Remedy:

This category means medicinal products, whose constituents have natural origins. But they may not be purified or significantly modified by chemical or biological method. They must be suitable for home cure in accordance with well-proven tradition. This category product can be sold outside of registered pharmacies, however, a label related to efficacy and the reduction effect on clinical symptoms is not allowed. Examples are: 1) vitamins and minerals which may be lacking in one's diet, 2) polyunsaturated fatty acid, 3) preparations to improve activity, 4) general supplemental preparations, 5) diet preparations and 6) preparations to treat osteoporosis. A new product may not be introduced onto the market until it has been approved by the Medical Products Agency.

2.3.4 The Netherlands

The Code of Practice-Assessing Scientific Evidence of Health Benefits stated in Health Claims on Food and Drink products, was established in 1998. It is a self-imposed standard based upon collaboration between the industrial society, consumer groups, scientific organizations, and the government.

A Health claim is defined as follows: "A direct or indirect or implied claim that a food carries special qualities which improve or maintain the users health." The scientific evidence for Health Benefits is assessed using the following criteria:

(1) The evidence must be based on relevant scientific data on human subjects.

- (2) The evidence must apply to a product or product group. Evidence proving the effectiveness of an ingredient or substance only will not be accepted.
- (3) Minor product variations which do not affect the claimed benefits - such as different flavours - do not require a reassessment of the effectiveness.
- (4) The data must concern normal use by the target population and the product must carry a herein relevant to that target group.
- (5) The Health Benefit must not dash with dietary guidelines, as laid down in publication by the former Nutrition Council and the Health Council and in similar international publication.

The applicant requests the Netherlands Nutrition Centre (NNC) to initiate and coordinate the assessment procedure. The applicant requests NNC to initiate and coordinate the assessment procedure. As soon as the NNC has received the application form, a panel of experts shall be appointed by NNC consultation with the applicant. The panel shall give its decision no later than 3 months following receipt of the dossier. The applicant is requested to provide the panel with further information regarding the health benefits and the scientific evidence. The panel shall attempt to reach a unanimous decision. On failing to do so the panel base its decision on a majority vote. In that case, minority opinions may be cited in the final report. The panel shall send a draft copy of assessment report to the applicant. Within two weeks the applicant make comments on the final report. On receipt of these comments, the final assessment report shall be drawn up. Should the applicant disagree with the panel's decision, he may request NNC to form a new panel within 3 weeks of receiving the assessment report. NNC shall allow third parties access to and provide a copy of the signed assessment report if the applicant can't has placed on the Dutch market products with a health claim.

2.3.5 Denmark

There is no plan that *Health Claims* will be approved for foods in the near future. This is because their consumers' group has a strong influence on the assembly, and they have been resisting the health claim. The guidelines for the *Nutrient Function Claim* are going to be proposed by the end of 1999. They contain the following idea.

Nutrient function claim is to be made for the nutrients generally lacking in the diet of Danish citizens, and not for all of vitamins and minerals cited in the Codex. The nutrients qualifying for application of the nutrient function claim include iodine, vitamin D,

and iron. Folic acid, selenium, and calcium are under discussion to be included in the nutrient function claim.

In the Codex meeting in Ottawa, they objected to establishing a working group to arrange the guidelines. They did not object to the discussion but mentioned the timing was too early to start preparing the guidelines

2.4 China

China has officially announced the administration method of health foods. They are approved for labeling a certain efficacy and are similar to the FOSHU of their Japanese counterparts. China implemented this on June 1, 1996.

The first chapter of this law, called the General Rules, states the following regulations.

Article 1: The present method is regulated by "The Chinese Food Sanity Act" to strengthen the supervision and administration of health foods and to guarantee the quality of the health foods.

Article 2: Health Foods mean foods obviously having some kinds of effects beneficial to one's health, which 1) are appropriate for specific people, 2) adjust body conditions, and 3) are not intended for treatment of a disease.

Article 3: The National Department of Sanity administers judgement regarding the approval system for health foods and produces an explanatory leaflet for health foods.

This law is related to Chapter 2: Approval for the judgement of health foods, Chapter 3: Production management of health foods, Chapter 4: Labels, explanatory leaflets, and publicity of health foods, Chapter 5: Supervision and administration of health foods, Chapter 6: Penal regulations, and Chapter 7: Supplementary provisions. There are 35 articles in those chapters in which detailed regulations are mentioned. Necessary conditions for the application of health foods are described in detail from Article 4 to Article 6 as follows:

Article 4: The following requirements should be fulfilled for the application of health foods.

- (1) Verify significant and stable effects beneficial to health based upon data from animal or human experiments.
- (2) All of the raw materials and products fulfill the standard of sanity for foods, and cause no harm to the human body acutely, sub-acutely, or chronically.
- (3) The prescribed composition and ingestion amount should be decided based upon scientific backing. The effective constituents should be included in the products with

efficacy clearly stated. If the effective constituents cannot be defined by current technology, the main raw materials should be clearly defined as they relate to beneficial health effects.

- (4) Treatment efficacy should not be advertised on the label, in explanatory leaflets, or by publicity.

Article 5: All of the foods defined as having beneficial health effects should undergo scrutiny and receive approval from the Sanity Bureau. The researchers should send applications to the Sanity Administration Division of each district where their company is located. After passing judgement, the health food will receive "certification of health food approval" by the Sanity Bureau, along with the approval number as "No. XXX of Health Food". With the "certification of health food approval", the health food can use the health food mark which is regulated by the Sanity Bureau.

Article 6: The following materials are required to apply for the "certification of health food approval".

- (1) Index of the health food.
- (2) Prescription, production conditions, and quality standards of the health food.
- (3) Pharmacological safety evaluation.
- (4) Efficacy evaluation for health benefits.
- (5) List of effective constituents of the health food, plus a qualitative or quantitative analysis coupled with the safety test methods used. Also needed is a list of main raw materials, as related to the beneficial health effects, in cases where the effective constituents can not be defined by the current technology.
- (6) Samples of the products and hygienic evaluation report.
- (7) Labels and explanatory leaflets to be used as samples for judgement.
- (8) Domestic and international reference materials.
- (9) Documents necessary for other regulations or for characteristic features of the products.

The following 12 items are shown as favorable effects that can be labeled on health foods after receiving approval through the judgement:

- 1) Immunoregulation effect, 2) anti-senescent (or aging) effect, 3) improvement of memory, 4) growth promotion, 5) anti-fatigue, 6) obesity reduction (body weight

reduction), 7) improvement of anoxemia, 8) anti-radiation effect (irradiation), 9) anti-mutation effect, 10) anti-cancer effect, 11) reduction of the blood fat, 12) promotion of reproductive system performance.

Further, the following 12 items are added for labeling of health foods on June 8, 1997, therefore, a total of 24 favorable effects on human health were officially announced:

1) Blood glucose adjustment effect, 2) gastric/intestinal adjustment function (the applicant should clearly state the substantial efficacy), 3) sleep promotion, 4) alimentary anemia improvement, 5) protection against chemically-induced hepatopathy, 6) lactation promotion, 7) cosmetic action (the applicant should clearly state the substantial efficacy), 8) improvement of vision, 9) anti-lead effect (ejection of poisoning), 10) purification action for moistening the throat, 11) blood pressure adjustment action, 12) osteoporosis improvement action.

(II) Market

1. Domestic market

1.1 Introduction

The concept of the physiologically functional food was defined for the first time in the Special Research Project supported by the Ministry of Education. This research was conducted from 1984 to 1986 and called "Systematic analysis of the function of food." At that time, the primary function of food was defined as the role of nutrition, the secondary function was defined as taste or sensory satisfaction, and the third function was defined as positive regulation of the physiological function. The new word "functional food" has been proposed as a food designed to show the third function effectively. In our study committee, the category of "functional food" is considered to have both scientifically-proven health benefits and appropriateness acceptable to an impartial third party. From this point, we consider FOSHU as a typical "functional food." It is approved by the Ministry of Health and Welfare to label its efficacy after scientific inspection. However, varieties of products that belong to the third function category exist in the Japanese market. These products range from high to low levels of scientific backing. It is practically difficult to select foods which can be categorized as functional food.

Therefore, in this section, we discuss what is on the market without limiting the topic "functional food." We classify foods into two categories; "healthy food" and functional food. We consider that "healthy food" is a food which has the efficacy of the third function as it is produced and sold, but without approval to show health effects on the label.

1.2 Functional food market in Japan

1.2.1 Potential market in view of an aging population and types of diseases

We will summarize the market for functional food in Japan considering social needs. In Japan, the population of people 65 years old or older will exceed 33 million in 2025, which will be 27% of the total population. After this peak, the elderly population will remain the same; however, the number of young people 0-19 years old will decrease. Therefore, the ratio of elderly people will continue to increase and reach 32.3 % of the total population. About 40% of elderly people live alone or live as a couple. Therefore, the ratio of families composed entirely of elderly people will continue to increase. The circumstances are such that the elderly society must be managed by the efforts of elderly people themselves (Source: "The outline of the medical service" issued by the Medical Service Material Survey Center in 1998). Also, national medical care cost reached 28.5 trillion Yen in the fiscal year 1996, an average of 227 thousand yen per person (Source: Indices of Welfare (supplement edition), "Trend of sanity of citizens", Welfare Statistics Association Foundation, Vol. 45, No. 9, 1998)

("Trend of National Sanitation" Vol.45, No 9, 1998 supervised by MHW)

Higher medical care costs are inevitable due to the increase of the elderly population and advancement of medical technology and science. Accordingly, maintenance of one's

health condition by life-style improvement has been considered a crucial objective in order to reduce the burden of medical care cost while maintaining high quality medical service. Therefore, a policy outline to positively evaluate function of food has been worked on. This includes reconsideration of the differentiation between food and drugs in the role of food, establishment of an individual evaluation system for patient food, and an investigation system of nutritious supplement food. Among life-style related diseases, the ones whose onset and advancement are directly related to eating habits, include insulin non-dependent diabetes, obesity, hyperlipidemia, hyperuricemia, cardiovascular disease, colon cancer, and so on. Table 3 shows major diseases which have at least an estimated one million patients each in Japan. Most of the diseases in Table 3 have been reported to have a relation to eating habits. Therefore, the hope of maintaining health through dietary improvement is substantial.

Table 3. Estimated patient number IN JAPAN FOR each major disease (1996)

Major Disease	Estimate number of patient (million)
Hypertension	7.49
Diseases of teeth and dental support structure	5.12
Diabetes	2.18
Cardiovascular disease	2.04
Cerebral vascular diseases	1.73
Cataract	1.58
Cancer (Gastric cancer and colon cancer)	1.36 (0.56)
Gastric ulcer and duodenum ulcer	1.16
Asthma	1.15

1.2.2 Market of FOSHU

By 1997, 100 items were approved as specified supplement food, and the number increased to 153 items in July 1999. Table 4 shows the market scale of each approved category of food in 1997.

The market scale for 1999 is estimated to reach about 200 billion Yen. This is because the approved items as of July 1999 include major marketing products of dairy industry companies and fermented milk-based drink companies as well as edible cooking oil.

Table 4. Market size of FOSHU listed according to health usage

Health purpose	Approved items	Sales amount (billion yen)
Food to affect gut intestine		
Use of lactic acid bacterium	8	97.9
Use of dietary fiber	24	11.9

Use of oligosaccharide	40	10.4
Food to regulate blood pressure	4	1.4
Food to improve absorption of minerals	8	9.2
Food to improve serum lipid concentration	12	0.03
Food to improve blood glucose level	4	0.67
Total	100	131.5

In July 1999, DENTSU CO., LTD. published "The current status of FOSHU" after their survey on the awareness of general consumers with respect to health consciousness and their understanding regarding purchasing specified supplement food. They reported that approximately 42% of the people claimed that they saw a sign indicating FOSHU, but only 25% answered that they recognized FOSHU. DENTSU also reported that approximately 15% of the people bought FOSHU, although only 3% knew the specifics regarding FOSHU. Although awareness of FOSHU content is low, about 40% of the people thought sales would increase with an aggressive information campaign. This answer suggests a lack of information for consumers has been the obstacle for popularization of FOSHU. (Source: "Food and Development", Vol. 34, 1999)

1.2.3 Market size for "healthy food" materials

The market scale for "healthy food" in Japan in fiscal year 1998 was estimated at approximately 750 billion Yen. Compared with the previous year, the increase ratio was only 1.5% due to reduction of purchases after an economic breakdown and market pressure for price reductions. Small "healthy food" stores have been declining; however, mail order specializing in "healthy food" sales has been rapidly increasing. In fact, a sale of FOSHU through specialized mail order is small. Their main sale items are "healthy food" in capsules or tablets, which use raw materials that lead consumers to expect health effects. Foods that claim health benefits have been increasing in the general market, however, an estimate of the market scale for such food as retail products is difficult.

Table 5 shows the components used for health-oriented food with a market scale of 10 billion Yen or more.

Table 5. Market scale of components for health-oriented food

	Market sale (billion yen)
Vitamin C	50.0
Chlorella	45.0
Royal jerry	45.0
Dietary fiber	40.0
Calcium	35.0
Vitamin E	35.0
Ginseng	20.0
Prune	20.0
Protein	20.0
Multi-vitamin	20.0
Supirmina	16.0
Galcinia	12.0
Kitosan	12.0
Bifidobacterium	12.0
プロポリス?	12.0
Nucleic acid	10.0
Enzyme	10.0
Leyss (Ganoderma bucidum)	10.0

Health Food Report, "Market trends of Health Oriented Food" 1998
Foods and Development, Vol 34, 1999

2. Overseas Market

2.1 Functional food market in the U.S.A.

The term "functional food" has not been legally acknowledged in the USA. Such products are classified as either food or dietary supplement food. Sometimes a term "nutraceutical" is used for a food which has physiological function and is useful to improve health. The estimated market scale for the nutraceutical food has been reported to range from 1.5 billion dollars to 77 billion dollars. The market scale in the USA has been difficult because the market size may include general processed foods which contain dietary fiber, vitamins and minerals, dietary supplement food or patient food. This is because function labeling has been allowed in the USA provided the components of specific nutrients are included in a food with more than the defined amount according to the Nutrition Labeling Education Act (NLEA). (Source: Information of Overseas Agriculture, Forestry and Fisheries Products", Vol. 79, 1997). Therefore, we estimated the market scale of food and drinks related to health care from two aspects: 1) Market scale of nutraceutical materials (Table 6), and 2) Survey results of companies that manufacture supplement food.

Table 6 shows the market scale of nutraceutical materials.

Table 6. Market scale of nutraceutical materials.

Category of materials	Estimated Sales (million \$)			Growth rate in one year	
	1987	1996	2001	96/87	01/96
Total material	876	1735	2530	7.9	7.8
Vitamins	288	485	650	6.0	6.0
Essential nutrients	236	410	555	6.1	6.2
Minerals	242	395	515	5.6	5.4
Herbs	32	320	650	29.2	15.2
Others	78	125	160	5.4	5.1

(Source: An article in "The Health Life Business")

According to data from the above article, the market size of food made from nutraceutical materials in table 6 was 47.8 billion dollars for general foods (including fluid diets for medical use), and almost 800 million dollars for nutritionally required foods such as low-calorie, diet food and cereals with dietary fiber. Another 6.4 billion dollars was spent on dietary supplements such as vitamins, minerals, and herbs, and 21.9 billion dollars went for nutrient enrichment drinks such as sports drinks and herb drinks.

The FDA investigated the economical impact of the Dietary Supplement, Health, and Education Act (DSHEA) and reported actual conditions of companies that manufacture dietary supplements (Federal Register 63 FR23623 April 29, 1998). According to the report, there are 850 of these manufacturing companies. Eleven companies have yearly sales exceeding 100 million dollars, which is 53% of the total sales for nutraceutical materials. Another 30 companies have sales from 20 to 100 million dollars, which accounts for 28% of total sales. And 809 companies have sales of less than 20 million dollars, which accounts for 19% of total industry sales. Their data shows sales shares for each business level and the average sales amount for companies with less than 200 million-dollar in sales (8 million dollars). Accordingly, the yearly sales scale can be calculated to be 34 billion dollars.

Although estimated market size is varied depending on the source of information, a rapid increase of the health care food industry has been shown in every report. The growth rate of the United States' health-care food industry in 1996 was reported at 25% growth from the previous year. The main reasons for this good rate of growth are: 1) increased income of consumers owing to a wave of economic prosperity and increased investments by enterprises, 2) establishment of the DSHEA which allowed companies to label effects beneficial to health on dietary supplements, and 3) an efficient distribution network. Also, the base of the expansion of the USA market is based on the fact that regulation of food labeling is considered related to education and economic policy. This is clearly seen in the FDA's attempt to calculate economical impact of the DSHEA.

2.2 Functional Food MARKET in other countries

Since the data to estimate market scale for functional food is insufficient in countries other than the USA, we introduce the concept or theory of a functional food market in China and Europe.

2.2.1 China

There is an approval system for "Health Food", whose meaning actually is "Food for Maintaining Health", in China, which is equivalent to that of FOSHU. (Please refer to the section on overseas laws and regulations). At present, 2,000 food items have been approved as "Food for maintaining Health". The foods have been sold in the same places as general processed foods in big grocery stores in china. The category includes forms such as a capsule or tablet, and forms close to general foods such as a biscuit or candy. Their effective constituents include not only natural remedies such as traditional ginseng, but also functional food materials such as EPA and DHA, which are distributed around the world.

2.2.2 Europe

In European countries, research on the third function of food and labeling health claims has been making progress mainly among member countries of the ILSI. However, it is only recently that food had been designed to fill the role of functional food.

The reasons for this are: 1) European countries tend to make much of the value of traditional food, thus the development of materials or components used only for food lags behind that of Japan and the USA, and 2) pioneers of the functional food market of Europe are giant multinational corporations. They have been unwilling to make the newly developed items into commercial products until they confirm with thorough verification evidence of benefits in terms of merit through a wide-ranging sales distribution system. Therefore, the leading products of the European functional food market are primarily dairy products such as yogurt. These products use probiotics (viable microbes such as lactic acid bacterium and bifidobacterium) and prebiotics (enteric bacteria growth promoting substance such as oligosaccharide).

Researchers for the giant food companies are aggressively participating in the ILSI associations in Europe. They are also actively attempting to reach a standardized level for the evaluation and labeling of European functional food for world distribution. Based on the business scale, research and development, and the market of East European countries, European food companies are expected to show a strong inclination to be the dominant force in the functional food market in the future.

(III) Scientific basis for the expression of health benefits

1. Introduction

Functional foods in Japan are classified into two types. First is a FOSHU for which the shape is apparently a food and is allowed to make health claims on the label. Second is a dietary supplement with a shape similar to a drug such as a tablet and a capsule. However, we still cannot clearly define the scientific endorsement for dietary supplement, because the definition and the system are presently under discussion.

Therefore, we only investigated FOSHU this time, since their labeling systems have been clarified already.

FOSHU is a food whose label expresses a health purpose, i.e., the benefits for the maintenance and improvement of human health. Among foods in Japan, a label expressing health benefits is allowed on FOSHU only. To consider the method of scientific backing for the expression of health benefits of food, we focused on FOSHU. We conducted surveys in terms of how the efficacy test on humans was performed with the most important factor being scientific verification.

2. Current status for the efficacy test regarding FOSHU.

2.1 Method of investigation

We researched reports of clinical trials which studied the relationship between food or components of food and maintenance / improvement of human health. These were mainly academic reports regarding FOSHU which had been legally approved. The outline was reported in the July 1998 report of ILSI-Japan.

2.2 Outline and issue of the investigation results

2.2.1 Summary of the clinical trial test

Many products are sold in the market as FOSHU approved to state on the label "maintain gut intestine." This is based on dietary fiber and oligosaccharide as active constituents. Also, there have been many papers which reported clinical test results on the efficacy of the responsible constituents. Most of these clinical tests were performed on healthy persons or persons healthy but are aware of a tendency toward constipation. Some of the clinical tests were performed on patients who had constipation. The forms of the test samples are usually in the shape of food, but are not the constituents alone. Usually statistical tests are performed to analyze the test results, and the standard condition of efficacy evaluation is based on the presence of statistically significant difference.

Regarding the scientific backing of food approved for labeling "prevents teeth from decaying", usually an in-vitro examination is performed using dental plaque collected from healthy people. This substitutes for a clinical trial, although clinical trial tests are performed in some cases.

In foods approved of labeling "appropriate for people who have relatively high blood cholesterol levels", clinical trials are performed on persons who are in a border line condition. They have no history of taking treatment medicines in spite of having relatively high cholesterol levels. In food approved of labeling "appropriate for people who have relatively high blood glucose levels", clinical trial tests are performed on both healthy adults and NIDDM (non-insulin dependent diabetes mellitus) patients. In food approved of labeling "appropriate for persons with relatively high blood pressure", clinical trial tests are performed on out-patients who have mild hypertension. In cases of life-style related diseases that are medically defined as being in the borderline zone, such as high hypercholesterolemia, diabetes, hypertension, attempts are made to perform clinical trial tests on human subjects who are in the borderline zone with such symptoms.

In food approved of labeling "mineral absorption", clinical trial test results of the absorption ratio of calcium and iron are used. Concerning to calcium, test subjects are postmenopausal women without any specific disease, and the responsible constituents are given doses as capsules or tablets. These capsules or tablets are taken along with ordinary drinks or light meals to make it similar to an ingestion style of food.

2.2.2. Problems in clinical trials

The first problem is selecting appropriate test subjects to conduct efficacy evaluation for FOSHU. The subjects of clinical trial tests varied from healthy persons to patients, and were different in each test case. If the nature of the test subjects was different, comparative study became difficult on the test results which were performed separately. In cases where the tests were performed on patients, the test results are based on the findings of diseased persons. To be logically precise, such test results will not be used as evidence of efficacy for healthy people, poor health people, or pre-diseased people who are the target customer for FOSHU. Therefore, we may consider that the food approved for labeling health benefits based on patient test results should belong to the category of foods for patients.

One reason why patients have been the subjects for clinical trial tests was the difficulty of proving the maintenance and improvement of health for healthy persons who were originally in good condition. Another reason is that the definition of poor health persons, who are most appropriate as the test subjects for FOSHU, was not clear. Therefore, in the future, it is considered necessary to clearly define the range of appropriate test subjects (poor health persons) for each labeling item. For example, in the case of a clinical test aimed at labeling items related to cholesterol, the test subjects may be selected from the borderline zone of people as defined in the guidelines from the Japanese Society of Arteriosclerosis.

The second problem is that the test methods for human clinical tests are not standardized. Confusion from the test methods might have been inevitable in the initiation period of FOSHU. However, since items have increased and the achievements have currently accumulated definitions of test methods that can obtain consensus both academically and internationally are desired.

As related to this second problem, the detection of statistically significant differences is considered important in human scientific tests. Sufficient numbers of subjects need to be prepared in order to ensure accurate statistical analyses. Many of the clinical tests for

FOSHU were performed on the appropriate number of subjects necessary for statistical analyses and the effectiveness was then evaluated based on the statistically significant differences. However, the appropriate number of subjects for the accurate statistical analyses varies in each test design. Therefore, we consider it necessary to standardize the test design for FOSHU in a certain range. Also, we need to consider that the number of subjects may vary according to the degree of effectiveness to enable statistical analyses.

We have researched and discussed problems pertaining to the efficacy test on humans. These tests are the main scientific backing for FOSHU. Now is the appropriate time to objectively investigate the guidelines for efficacy evaluation tests on humans. This will prove the labeling of health benefits occurs after accumulation of actual results for FOSHU. We consider it very significant to investigate "the ideal way" after reviewing these current conditions.

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