



PERSPECTIVES ON ILSI'S INTERNATIONAL ACTIVITIES ON FUNCTIONAL FOODS

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About ILSI / ILSI Europe

The International Life Sciences Institute (ILSI) is a non-profit, worldwide foundation established in 1978 to advance the understanding of scientific issues relating to nutrition, food safety, toxicology, risk assessment, and the environment. By bringing together scientists from academia, government, industry, and the public sector, ILSI seeks a balanced approach to solving problems of common concern for the well-being of the general public. ILSI is headquartered in Washington, DC, USA. Branches include Argentina, Brazil, Europe, India, Japan, Korea, Mexico, North Africa and Gulf Region, North America, North Andean, South Africa, South Andean, Southeast Asia Region, the focal point in China, and the ILSI Health and Environmental Sciences Institute (HESI). ILSI is affiliated with the World Health Organization as a non-governmental organisation (NGO) and has specialised consultative status with the Food and Agriculture Organization of the United Nations. ILSI Europe was established in 1986 to identify and evaluate scientific issues related to the above topics through symposia, workshops, expert groups, and resulting publications. The aim is to advance the understanding and resolution of scientific issues in these areas. ILSI Europe is funded primarily by its industry members.

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1. EXECUTIVE SUMMARY

The aim of this document is to summarise the achievements and contributions of ILSI in functional food science and its impact on the science base for functional foods and their regulation. The document identifies gaps and shortcomings in ILSI's current global efforts and proposes future priorities. It is intended to be read by ILSI stakeholders in academia, industry and government as well as by all those interested in the scientific basis for development of foods that contribute to a modern diet.

Improving diets and increasing physical activity are considered pivotal for improving health as well as reducing the risk of non-communicable diseases, including cardiovascular diseases, type 2 diabetes, obesity, osteoporosis and certain types of cancer. The World Health Organisation in its "Global strategy on diet, physical activity and health" as well as the European Commission and governments around the world consider diet and health as of the highest priority.

Against this background, consumer interest in diet and health is greater than even before. Consequently, consumer demand has grown for information about food and health and for specific foods that provide health benefits beyond normal nutrition. Thus a firm scientific underpinning of claims for health-associated functions of foods is important for all stakeholders concerned: governments, industry, scientists and consumers.

Key Activities and Achievements

The concept of "functional foods" has its origins in Japan. ILSI has been active on functional foods in Japan since 1991 and there are now task forces on this topic in ILSI branches worldwide. There is no agreed definition of functional foods but in this report the term refers to foods that are consumed as part of a normal food pattern and that have beneficial effects on body functions that go beyond adequate nutritional effects and that are relevant to an improved state of health and well-being and/or a reduction of the risk (not prevention) of disease.

The principal contribution ILSI has made to the discipline is to provide an international forum for sharing information, for discussion, debate and, importantly, for consensus building between the various interested parties. ILSI's fundamental role is to bring together scientists from government, academia and industry to address topics of mutual interest. Organising activities in genuine partnership with agencies represented by these scientists has been critical to the success of the work on functional foods, particularly in relation to the scientific basis for regulation. The two EU concerted action programmes lead by ILSI Europe are an excellent example of consensus building. However, in practice, harmonisation of scientific and regulatory approaches around the globe needs further improvement.

ILSI has contributed to building the science that underpins the regulatory framework in Asia, Europe, The Americas, Australia and New Zealand as well as at the international level through Codex. Some of the debate has been around the definition and classification required for regulation and a great deal of discussion has been around the scientific substantiation of claims and, in Asia, the evaluation of the safety of functional foods. ILSI has convened three global and many regional symposia and workshops on this topic as well as on the basic science of the food health relationships involved. ILSI has also organised many conferences

exploring the biological properties of a wide array of foods and food components that are the foundation of functional food science.

Future and Recommendations

Functional food science is a complex field and it would be misleading to believe that all possible scientific aspects could be addressed by ILSI task forces that are specifically focused on functional foods (ILSI FFTF) or indeed by all the ILSI task forces together. There are a number of gaps in ILSI's activities to date, notably in the fields of food technology and consumer sciences but there are also some important opportunities to complete the science base for regulation and to explore emerging areas such as biomarkers and biomics. ILSI must consider these gaps and opportunities in the context of the breadth of this field and prioritise its objectives and activities appropriately. Some activities may be best left to other task forces or to third party organisations. It will also be necessary for ILSI FFTF to collaborate with other task forces as well as with external scientific groups (e.g. learned societies and scientific trade groups).

Four key priorities were identified by Branches that met in January 2007. In addition, if ILSI continues to focus on functional food science as a global priority improved integration of activities is required.

Global Harmonisation of Substantiation

While it is true that there remains a lack of global consensus on the definition and classification of functional foods and of nutrition and health claims, this is largely due to a difference in regulations and in philosophy about the role of functional foods and the tensions that exist worldwide between scientific progress and consumer protection. However, it should be possible to achieve global consensus on criteria for the scientific substantiation of claims. ILSI Europe's PASSCLAIM and the work of ILSI Southeast Asia (SEA) Region have lead the way and it is important that ILSI continues to disseminate relevant information on these projects, including providing global ILSI input to the Codex deliberations.

Science Base of Regulation in Practice

ILSI Europe and ILSI SEA Region have both planned projects to test the practicality of their criteria for the substantiation of health claims. These projects should progress jointly to foster international co-operation and harmonisation. ILSI could also encourage investigators to share their experimental protocols with others by adding information in available databases, including PDQ (Physician Data Query) if the focus is cancer (<http://www.cancer.gov/cancertopics/pdq/cancerdatabase>), or, for more general human studies, the Clinical Trials database (<http://clinicaltrials.gov>).

Scientific Assessment - Biomarkers

Biomarkers are vitally important areas of research and validation of new markers of exposure (intake) are needed as well as those for delineation of health or disease endpoints. Developments are likely to be rapid and exciting as they impact many facets of the life sciences. For the FFTF, there is an opportunity to develop, using modern computing technology, a database to document functional ingredients in foods and food components together with analytical methods, relevant biomarkers of exposure and effect, methodology for biomarker measurement and references to clinical and other studies that support (or do not support) that there is a biological effect. It is also important to foster collaboration around the

world to encourage harmonised methodologies and standards. ILSI needs to keep track of these developments through a wider range of task forces than simply those working on functional foods and should be prepared to summarise developments, identify applications for the new technologies, to identify gaps and to keep their target audiences up to date.

Consumer Understanding of Health Claims

While ILSI does not target the consumer directly with its publications, a better understanding of consumer science is important. The new structure of clusters within ILSI Europe and SEA Region with a focus on the consumer will no doubt aid progress in this area. The ILSI Europe Consumer Science Task Force project on Consumer Understanding of Health Claims has developed a scientific basis for the measurement of consumer understanding. ILSI could also use the new methodology to examine consumer understanding of benefit-risk scenarios, an important topic in more than just the functional food field. Valuable links can be forged with consumer organisations as well as with communications groups such as the International and regional Food Information Councils (IFIC, EUFIC, AFIC).

Integration

Functional food science is a complex field and not all aspects can be addressed by ILSI FFTF. It will therefore be necessary for them to collaborate with other task forces as well as with external scientific groups. It is thus recommended that each branch appoint a functional food co-ordinator with key objectives, to improve global integration, and co-ordination and communication.

Other Opportunities

Food Technology

ILSI FFTF should join with other relevant ILSI task forces and/or other science/technology groups such as The International Union of Food Science and Technology (IUFOST). Engaging in such an activity can identify synergies between different food process streams and gaps in information that might be required by industry, regulators or consumers. New technology such as nanotechnology may well impinge on functional food development so it will be important to help regulators understand the benefits and risks of such technology and the ways in which they can benefit industry and ultimately the consumer. Enabling educators and communicators to provide information to the consumer will help improve confidence in new technologies.

Foods and Drinks - Understanding Plant Components

There is a need to understand the protective effects of the estimated 25,000 bioactive components in plant foods in order to better guide the future directions for plant breeding, product innovation as well as public health advice – which already include advice to eat more plant foods. The project mentioned above, to test and refine the PASSCLAIM criteria, will focus on polyphenols and will attempt to assess the amount of intake of polyphenols required to exert claimed effects as well as to identify *in vitro* techniques that could be used to screen polyphenols. If a project on biomarkers is initiated, exploiting modern computer techniques to develop a database on biomarkers, these techniques could also be used to document data on plant components. A combined project should thus be of interest to ILSI Europe, ILSI SEA Region and ILSI Japan (for their work on teas). Ultimately, this would have worldwide application.

Scientific Assessment - Biomics

With the rapid advances in our understanding of nutrigenomics (the impact of our genes on our biological responses) and nutrigenetics (the effect of nutrients on gene expression) and the potential for the application of metabolomics, it is essential to assess the impact of these findings on the science-base of functional foods, particularly as it relates to scientific assessment. ILSI could seek opportunities to co-ordinate international groups in their collaboration or ILSI Europe could identify partners to submit project proposals under the European Commission Seventh Framework Programme. ILSI Europe and ILSI Japan should consider a workshop on metabolomics in the next five-year plan.

Scientific Assessment - Intake Exposure

ILSI task forces have contributed a great deal to the topic of exposure to (intake of) food components. There may be synergies for the ILSI FFTF with current activities of other task forces including the ILSI Europe Addition of Nutrients to Food Task Force and the ILSI Europe Novel Foods Task Force.

Biological Effects - Benefits and Risks

Functional foods provide specific health benefits. However, in some cases, the ingestion of foods or food components can pose a risk perhaps to some population groups. The outcome of a new EU Specific Support Action BRAFO project (Benefit Risk Analysis of Foods) to establish a common unit of measurement for comparing such benefits and risks quantitatively to improve the benefit-risk analysis process will find important application in functional food science.

Benefits and Life Stages

There is still much work to be done in terms of understanding the biological effects of functional foods so that foods can be identified or formulated for target conditions at different life stages, for example mental function during ageing. ILSI Japan has been active on ageing and its plans to make more information available in English should be pursued. ILSI should sponsor systematic reviews of these fields to ensure the best interpretation of the plethora of data that is available in the literature.

Science Base of Regulation - Nutrient Profiling

Nutrient profiling is the classification of foods for specific purposes based on their nutrient composition. A profiling scheme is being developed in the EU to be applied to foods bearing health claims. It is of paramount importance that such schemes are science-based and have a common basis around the world. Thus ILSI Europe should extend the work to validate the food-based approach discussed at their April 2006 workshop (Asp et al 2007).

Target Audiences

ILSI FFTF should always consider publication related to its activities and should find cost effective ways to disseminate information more widely, effectively and quickly for example on the internet or by making use of e-publication opportunities. ILSI should try to evaluate the benefit of their activities and publications to their target audiences. New audiences might also be identified, for example those in health economics could be interested in work on the cost/benefit aspects of functional foods. Finally, ILSI should continue to build on its core role in bringing together scientists from government, academia and industry to reach consensus on all relevant aspects of the science.

2. INTRODUCTION

Improving diets and increasing physical activity are considered pivotal for improving health as well as for reducing the risk of non-communicable diseases, including cardiovascular diseases, type 2 diabetes, obesity, osteoporosis and certain types of cancer. Though many people intend to eat a healthy diet they fail to do so mainly for the reasons of busy lifestyle but also because many associate healthy diets with poorer taste or long preparation times. This has created a demand in the developed world for convenience food as well as for foods that provide health benefits.

There is as yet no agreed legal definition of functional food. The Japanese regulatory authorities were the first to acknowledge this class of foods and they established the category “Foods for Specified Health Uses” (FOSHU) in 1991 (see Section 3) and the USA is currently considering a functional food category. In a recently commissioned report for The Food and Agriculture Organisation of the United Nations an international definition for functional foods is called for (FAO 2007). There are many “working” definitions but in this report the term functional foods refers to be foods that are consumed as part of a normal food pattern and that have beneficial effects on body functions that go beyond adequate nutritional effects and that are relevant to an improved state of health and well-being and/or a reduction of the risk (not prevention) of disease.

The term "functional foods" may have gained prominence only in recent years, but in Asia, foods with functional properties have been regarded as an integral part of some cultures for centuries. Among the Japanese and Chinese, for instance, it is believed that foods and medicine are of equal importance in preventing and treating diseases; that foods and medicine originate from the same source, are based on the same basic theories and have the same uses. It is also believed that the functionality of foods is found in whole foods rather than in their individual components. Elsewhere in the world there are much clearer distinctions between foods and medicines both from a conceptual point of view and from a regulatory perspective. In North America, foods and medicines are viewed as distinct in their roles and functions and there are clear demarcations in legislation. Likewise in Europe there is a defined legal boundary and when there is uncertainty about the classification of a product, the law regards it as a medicine if it is deemed medicinal claims are made. It is nevertheless interesting that in many parts of the world ancient medical practices document the use of foods for medical purposes.

Consumers identify foods to meet their needs by the claims that are made in the marketing of such foods. The increased interest in the functional properties of foods has therefore led, over the last 15 years, to considerable investment in research and development by government, industry and academia in order to pursue a better understanding of food:health relationships. It has also lead to discussion and action worldwide to regulate both the foods and the claims that are made for them. Such regulatory initiatives have an impact on both the industry and the consumer and are discussed below in some detail.

Claims may be based on new or on existing insights into effects of food components on physiological functions, health and disease. The scientific underpinning of these health-associated functions is critical for all stakeholders involved and there is only an opportunity

to benefit consumers and companies alike if this knowledge is handled in a proper and appropriate way.

The aim of this document is to summarise the achievements and contributions of ILSI in functional food science and its impact on regulations. The document identifies gaps and shortcomings in ILSI's current global efforts and proposes future priorities. It is intended to be read by ILSI stakeholders in academia, industry and government as well as by all those interested in the scientific basis for development of foods, which contribute to a modern diet.

The information in this document was to a large extent supplied by the ILSI branches and secondary sources such as available literature, articles and websites of other organisations.

2.1. WHO Global Strategy on Diet, Physical Activity and Health

In order to place this report in a relevant context it is important to consider the current emphasis on diet and health. In May 2004, the World Health Organisation (WHO 2004) published a report on a "Global Strategy on Diet, Physical Activity and Health". The report states that the burden of non-communicable diseases has rapidly increased and lack of sufficient actions to prevent these diseases presents a major challenge to global public health.

This global strategy has four main objectives:

- to reduce the risk factors for non-communicable diseases that stem from unhealthy diets and physical inactivity by means of essential public health action and health-promoting and disease-preventive measures;
- to increase the overall awareness and understanding of the influences of diet and physical activity on health and of the positive impact of preventive interventions;
- to encourage the development, strengthening and implementation of global, regional, national and community policies and action plans to improve diets and increase physical activity that are sustainable and comprehensive and actively engage all sectors, including civil society, the private sector and the media;
- to monitor scientific data and key influences on diet and physical activity; to support research in a broad spectrum of relevant areas, including evaluation of interventions; and to strengthen the human resources needed in this domain to enhance and sustain health.

The global strategy proposed by the World Health Organization (WHO), identifies the food industry and retailers as potential partners in promoting healthy diets. The WHO not only highlights the type of overall dietary change it sees as necessary but also refers to "functional foods" as foods aiming for specific health purposes, including mental and physical performance. Thus within the global strategy, functional foods could play an important role in the risk-reduction of non-communicable diseases and by providing benefits beyond usual nutrition and in optimising health and general well-being.

Prior to the WHO initiative, many national governments as well as the European Commission have increased efforts to combat the burden of non-communicable diseases. In March 2005, the European Commission launched its Platform on Diet, Physical Activity and Health to provide a common forum at European level for all interested actors to drive ahead initiatives to combat the problem of overweight and obesity.

3. ILSI ADDED VALUE – FROM 1995 TO 2007

The concept of “functional food” has its origins in Japan where a regulation was introduced in 1991 to establish a procedure for the approval of health claims on “Foods for Specified Health Uses” (FOSHU). ILSI Japan has thus been active on the topic of Functional Foods since 1991 and especially since 1993 when the first FOSHU product was approved. ILSI Europe was the first branch to establish a task force on functional foods in 1996, closely followed by ILSI Japan in the same year. In contrast to Europe and North America, Asian countries have regarded foods with functional properties as an integral part of their culture for centuries and they still today have a prominent place in the diet. The differences between the regulatory approaches to functional foods in key regions around the world are discussed in Section 3.2 below.

The principal contribution ILSI has made to the Functional Foods discipline is to provide an international forum for sharing information, for discussion, debate and, importantly, for consensus building between the different interested parties. ILSI’s fundamental role is to bring together scientists from government, academia and industry to address topics of mutual interest. Organising activities in genuine partnership with agencies represented by these scientists has been critical to the success of the work on functional foods, particularly in relation to the science base of regulations. Examples of the wide range of stakeholders involved with ILSI activities on functional foods are listed in the box.

Stakeholders

- Food and Agriculture Organisation
- World Health Organisation
- Codex Alimentarius
- European Commission
- National government agencies
- Consumer Groups
- Food Industry

The theme of functional foods has not only involved participants from amongst ILSI’s scientific network but has also involved non-scientists, particularly from government agencies and some consumer groups, who need to have a broad understanding of the scientific principles involved. The needs of this group are to some extent met by publications such as ILSI Europe’s Concise Monograph on Concepts of Functional Foods (Ashwell 2002), which provides a summary of the key themes around functional foods in a less technical format than the peer-reviewed publications aimed at a scientific audience. A further Concise Monograph was published in 2008 (Howlett 2008).

In this section, the added value of ILSI is considered under the following five headings. For further information on past ILSI activities on function foods see <http://www.ilsi.org/>

- Gathering and Sharing Information
- Reaching Consensus on the Scientific Basis for Regulation
- Scientific Advances
- Industry Developments
- Consumer Aspects

3.1. Gathering and Sharing Information

There have been three Global Conferences between 1995 and 2007. The First International Conference on East-West Perspectives on Functional Foods was held in Singapore in 1995 at the instigation of ILSI Southeast Asia (SEA) Region but with support from a number of branches. Partners for the meeting included FAO and WHO as well as the Ministry of Health in Singapore and the International Union of Food Science and Technology. The broad programme shared information on the new concept of functional foods in the East and the West, on health benefits of traditional and novel foods and ingredients from around the world and also explored the topics of safety evaluation, regulation, the scientific substantiation of claims and the consumer's perspective. The proceedings were published in *Nutrition Reviews* (1996).

The second International Symposium on Functional Foods: Scientific and Global Perspectives was led by ILSI Europe and held in Paris in 2001. Once again there was support from ILSI International and branches, in partnership with The French Ministry of Research and the European Commission Directorate General (DG) Research. The aims of the conference were to review the scientific basis of functional foods and to identify areas of agreement and disagreement, to identify unifying concepts and illustrate them with relevant examples, to review current scientific support for biomarkers to link functional food consumption to quality of life and/or health, to review the communication requirements from a scientific, consumer and regulatory point of view and to identify new trends in functional food science. The proceedings were published in *British Journal of Nutrition* (Saris et al 2002). Also published was an ILSI Europe Report (Verschuren 2002) setting out the key messages from the conference, in particular related to the topic of biomarkers and the variability in human genetics, and setting the scene for the future.

The third International Symposium in May 2007 in Malta, was organised by ILSI Europe, in collaboration with the Malta Standards Agency, the University of Malta and ILSI SEA Region, and provided an opportunity for interdisciplinary dialogue on the status and the future of scientific substantiation of health claims; consumer understanding, behaviour and communication; the impact of regulation on health claims and innovations in functional foods and the future opportunities and challenges for functional foods. A short perspective on the event was available shortly after the meeting (Madsen 2007) and a more detailed summary of the symposium published in 2008 (Binns and Howlett 2008). Some selected papers from the symposium proceedings together with the summary report will be published in a supplement to the *European Journal of Nutrition* in the second half of 2009.

The ILSI branches have organised many conferences ranging from international symposia to focused local seminars. The main focus of these has been on sharing information and ideas on the different approaches around the world to the regulation of functional foods and health claims; on the scientific substantiation of health claims; on the science behind specific ingredients or food groups or their impact on body systems or function; on the application of knowledge to food fortification. Many of these events have been organised in the context of the activities described in the following sections.

3.2. Reaching Consensus on the Scientific Basis of Regulation

There is no doubt about the importance of consensus amongst scientists to ensure a sound science base for regulation, to provide a consistent approach to the assessment of that science and to build consumer confidence. ILSI has contributed greatly to building the science that underpins the regulatory framework in Asia, Europe, The Americas, Australia and New Zealand as well as at the international level through Codex. (Functional Food Science in Europe (FUFOSE) and Process for the Assessment of Scientific Support for Claims on Foods (PASSCLAIM) and a series of initiatives in SEA Region as well as inputs to the Codex Alimentarius Commission are of particular note and are detailed in the sections below).

Definitions

Some of the debate has been around the definitions and classifications required for regulation but despite work such as FUFOSE and ILSI SEA Region efforts to have an Asian position on functional foods, no global consensus on the definition of “functional foods” or “functional ingredients” has emerged. Indeed, most countries have no such specific food category although the USA has this option under consideration. Numerous definitions are used resulting in confusion as to which foods or ingredients are included. Further, it is still debated whether nutrient-fortified foods can be regarded as “functional foods”. Some fortified foods are used to combat or reduce the risk nutrient deficiency (for example fortified wheat flour, iodinated salt or iron fortification) whereas some may be intended to provide benefits that go beyond the traditional nutritional requirements (for example folic acid to reduce the risk of neural tube defects). As science develops and more is known about day-to-day foodstuffs that have functional properties, definitions become further blurred. This is not only of theoretical and rhetorical concern, but has direct practical and legal implications.

Claims

Rather than trying to define “functional foods”, it is perhaps preferable to define and categorise the claims made about foods. The EU, the USA and Codex have all taken this approach, based in some part on the work of ILSI Europe and ILSI SEA Region. Although this has led again to several definitions of claims but no clear global consensus, this approach does look more promising for global harmonisation. Widely agreed, at least in the western world, is that foods cannot be claimed to prevent, treat or cure disease - that is the realm of medicines.

A comparison of various approaches to health claims regulation is provided in Table 1.

Table 1: Comparison of International Approaches* to Health Claims

	Aus/NZ	Brazil	Canada	Codex	EU	Japan	USA
Nutrient Function claim	✓	✓	Biological Role Claims	✓	✓	✓	✓
Enhanced function claim	High level claim	✓	x	Other function	✓ Not defined	✓	x
Disease risk reduction claim		✓	✓	✓	✓	✓ (added in 1996)	✓
Regulation for pre-market approval of health claims	✓ (High level only)	✓	✓	n/a	✓	✓	✓
Safety assessment requirement	In separate regulation	✓	In separate regulation	in draft guideline on substantiation	In separate regulation	In regulation	In separate regulation
Process for substantiation (separate code)	✓	✓	✓	✓	✓	✓	✓
Mandatory wording of disease risk claims	Possibly	✓	✓	n/a	Possibly	✓	✓
Start date of code / regulation	2010	1999	2004	At step 2/3 in 2007	2007	1991 (revised 2001)	1990 1997 2000 2003
No. of health claims approved	5 generic** (high level)	12 generic claims	5 generic claims***	n/a	Main lists from Jan 2010	590 product specific claims (2006)	14 generic claims

*See end of References (Section 6) for references and/or links to the legislation or guidelines.

** Five generic claims reviewed and accepted as “convincing”. These and any additional ones reviewed and accepted will be published in the forthcoming Standard

***Approval for product specific claims may also be sought

n/a not applicable

In order to regulate claims, it is also necessary to agree on criteria for the scientific basis of health claims and this topic has also been the subject of international discussion. ILSI Europe's PASSCLAIM and ILSI SEA Region's workshops form the core of ILSI's contribution. A comparison of the approaches by these two ILSI branches and by Codex is provided in the Annex.

Safety

Finally, the safety of functional foods has to be considered. This is addressed by standard, separate food safety laws in the Americas and in Europe (including "novel foods" legislation) as well as in Australia and New Zealand. The USA is likely to place greater emphasis on safety as it considers the regulation of functional foods. In Japan and Asia the safety of functional foods is generally addressed alongside claims on a case-by-case basis and has thus been a topic of interest to ILSI SEA Region. The draft Codex guidance on the substantiation of health claims recommends consideration is also given to safety in terms of exposure to claimed ingredients.

3.2.1. Asia and Japan

In Asia and especially in Japan, the approach had been to regulate individual foods that are regarded as having functional properties (and thus the claims made on them) on a case-by-case basis. ILSI SEA Region has been extremely active in bringing together players across SE Asia.

In 2002, a survey on functional foods was conducted by ILSI Southeast Asia amongst the Regulatory Agencies of eleven Asian countries (China, Indonesia, Japan, Malaysia, Myanmar, the Philippines, Singapore, South Korea, Taiwan, Thailand and Vietnam). Under this survey, the term "functional foods" is defined as: "foods that possess physiological or health benefits beyond basic nutritional functions".

Findings of the survey (Tee 2003) showed that there was no consensus among the respondents on the definition or usage of the term "functional foods". Only Japan, China and Taiwan have regulatory systems that regulate foods falling wholly or partially within the scope of the survey's definition of functional foods. In China, South Korea and the Philippines the term "functional foods" was used to include dietary supplements in pharmaceutical dosage forms.

In the remaining countries (Indonesia, Malaysia, Myanmar, Singapore, Thailand and Vietnam), the findings showed that there were no regulations on functional foods. Although these six countries recognise functional foods as an important area that requires further development and regulation, none has enacted specific regulations for such foods.

As the survey findings revealed a lack of consensus amongst the region's countries, ILSI SEA Region convened two Asian workshops on functional foods in 2003 and 2004, drawing together regulators and scientists from around the Asia region, including regulators and scientists from Australia and New Zealand. The workshops were able to reach broad agreement on the form and properties of functional foods and the need for safety and benefits to be scientifically proven. The conclusions of the survey and these two workshops were published in *Functional Foods in Asia: Current Status and Issues* (Tee 2004) and compared with approaches by Codex and by other countries worldwide. An Asia Expert Consultation was also organized in December 2005 to briefly review the agreements on the Asian Position

on Functional Foods as well as to establish the guidelines for scientific substantiation for nutrition and health claims and safety evaluation of functional foods that were discussed at the 2004 workshop. In July 2006, the regional regulators were invited back to the 3rd Asian Workshop on Functional Foods to help review these guidelines. It was anticipated that these guidelines would be used by the regional regulatory agencies to develop their national framework for substantiation of nutrition and health claims.

As a basic step towards the common understanding, the following were proposed to be the essential attributes or characteristics of functional foods:

- (i) be in conventional food forms and possess sensory characteristics including appearance, colour, texture, consistency and flavour;
- (ii) contain nutrients and/or other substances that confer a physiological benefit over and above their basic nutritional properties. These foods should not be intended for medicinal or therapeutic use;
- (iii) possess functional benefits that can be scientifically proven and accepted by the relevant regulatory authority;
- (iv) possess functional benefits that can be derived by consuming normal amounts of the foods;
- (v) be whole foods that contain ‘functional’ nutrients and/or other substances that may be naturally present or be added to the food;
- (vi) contain adequate amount of ‘functional’ nutrients and/or other substances that produce the claimed effect/in relation to the claimed effect; and
- (vii) have been proven to be safe during long term usage by the intended target population, based on existing science.

Further, the term “functional food”:

- (i) should not be used for food components in isolation. The food components would be the nutrients and/or other substances conferring the functional properties and would be best referred to as “functional components”. If these functional components are extracted from the food and presented in pharmaceutical dosage forms, they may be called “nutraceuticals”;
- (ii) should not be used for dietary supplements; and
- (iii) may be used for fortified foods, if the fortification or words of similar meaning is to augment a constituent normally present in a food or to add a constituent not normally present in the food in order to confer a property beyond its natural nutritional attributes.

The guidelines for the scientific substantiation of claims developed by ILSI SEA Region (Tee 2007) were based on documents on PASSCLAIM (Process for the Assessment of Scientific Support for Claims on Foods) by ILSI Europe, Proposed Draft Recommendations on the Scientific Basis of Health Claims from Codex (CX/NFSDU05/27/9, July 2005) as well as recommendations from 2nd Asia Region Workshop on Functional Foods. New information from the revised Codex document on the scientific basis of health claims (CX/NFSDU 06/28/7, June 2006) was also used as a reference. The final set of the guidelines for scientific substantiation of claims is tabulated in the Annex alongside a comparison with PASSCLAIM and the draft Codex guideline. It is encouraging that there is a great deal in common between these approaches, which may in part be due to ILSI’s global scope.

A particular focus in Southeast Asia has been the safety of functional foods because many functional ingredients are considered to be on the borderline between foods and traditional medicines. ILSI SEA Region has also been instrumental in the decision to convene an FAO/WHO workshop on Functional Foods: Safety and Regulatory Aspects in the Republic of Korea in September 2004. The ILSI SEA Region's Expert Consultation in December 2005 and the 3rd ILSI SEA Region's Asian Workshop on Functional Foods also addressed the safety and nutritional safety evaluation of functional foods. The conclusions were that while functional foods or components must fulfil the minimum safety requirements for food, as set out in the national legislations or in their absence, in the Codex Alimentarius, there are occasions where additional data are required (Tee 2007).

A rapid growth in the functional food market in Korea prompted the local government to develop a new regulatory framework and management system, the Health Functional Food Act (HFFA), which was launched in August 2004. The HFFA was established to safeguard public health and to protect consumers from misleading claims and false labelling. By requiring thorough scientific substantiation of health claims it will help the development of the functional food industry as well as facilitate the discovery of new physiologically active functional foods/food components. According to the HFFA, functional foods are limited to dietary supplements by definition¹ and currently 37 types of certified generic health functional foods have been included in the Health Functional Food Code of Korea. In addition, product-specific health functions for foods can be petitioned to the Korea Food and Drug Administration for certification.

The Korean government wants to continue to develop evidence-based regulation on functional foods, which makes the scientific activities of ILSI of increasing importance. In response to this need, in February 2006, ILSI Korea branch re-activated their Scientific Committee on Functional Foods (SCFF) consisting of 14 experts from academia and the food industry and chaired by an academic. Some of the major issues that the SCFF has identified as for future activities are scientific substantiation of health claims, development of biomarkers, safety assessment and a science basis for harmonized regulation as well as consumer understanding and behavioural science. The SCFF will work closely with experts from government, academia and industry to provide sound scientific information and platforms for communication leading to consensus among the stakeholders.

3.2.2. Europe

The emphasis in Europe is on the regulation of the claims rather than on the regulation of the foods themselves. (The safety assessment of all foods is addressed by separate regulations). Food legislation does not allow claims about prevention, treatment or cure of diseases as such claims are confined to medicinal products. Accordingly, the mention of food effects in relation to disease on food labels or in other promotional material has been regarded as a medicinal claim. However, disease risk reduction is a well-established concept in nutrition and is indeed a basis for official dietary recommendations. A major breakthrough in European food legislation is that the 'Regulation on nutrition and health claims made on foods', includes a procedure to approve claims for a reduction in disease risk (EU 2006).

¹ Health Functional Foods are defined in the Health Functional Food Act of Korea as a processed food used with intention to enhance and preserve human health by physiologically functional ingredients and/or components in forms of tablet, capsule, powder, etc.

ILSI Europe led two successful programmes on functional foods funded by the European Commission (see below). This has ensured the involvement of the Commission in all the processes developed. Thus, the outcomes would be given due consideration in developing European legislation relating to claims. In addition these results would provide a stimulus for innovation in product development within the industry. Both programmes have already had and will also have wide impact within the European Union and elsewhere in the future.

The European Commission Concerted Action on Functional Food Science in Europe (FUFOSE), which was co-ordinated by ILSI Europe, established a science-based approach for evaluating functional foods. The project documented (Bellisle et al 1998) the scientific evidence that foods, nutrients or other substances positively affect physiological functions and/or reduce the risk of certain diseases.

FUFOSE has contributed significantly to the worldwide debate on definitions of claims. The consensus document (Diplock et al 1999), which was the final outcome of the concerted action, proposed a classification of claims to go beyond the accepted nutrient content and nutrient function claims. It defined ‘enhanced function’ and ‘disease risk reduction’ claims and outlined the requirements for scientific substantiation of claims.

Enhanced function claims were defined in FUFOSE as:

“claims that concern specific beneficial effects of nutrients and other substances on physiological and psychological functions or biological activities beyond their established role in growth, development and other normal functions of the body.”

While enhanced function claims were previously recognised by the Council of Europe and are also included in the Codex Alimentarius Guidelines (CAC/GL 23-1997, Rev. 1-2004) as “other functions claims” they are not included amongst the definitions in the EU Regulation on nutrition and health claims made on foods (Table 2).

However, the dotted lines in Table 2 indicate that there is no absolute delineation between “nutrient function claims” on the one hand and “enhanced function/other function claims” on the other hand. A “new” function of a nutrient may be regarded as enhanced/other function until generally recognised as a “nutrient function claim”. A function of a non-nutrient would be regarded as “other function” according to Codex. Both would be regarded as simply a “health claim” under the EU regulation (EU 2006).

Table 2 - Health claims classification according to FUFOSE, Council of Europe, Codex Alimentarius, the EU Regulation and USA

FUFOSE (1998)	Council of Europe (2001)	Codex Alimentarius (2004)	EU Regulation (2006)	USA (2006)
Nutrient function claims not considered ----- A. Enhanced function claims	Nutrient function claims not considered ----- A. Enhanced function claims	Nutrient function claims ----- Other function claims	Health claims describing or referring to the role of a nutrient or other substance in growth, development and the functions of the body*	Structure function claims
B. Disease risk reduction claims	B. Disease risk reduction claims	Disease risk reduction claims	Health claims related to disease risk reduction	Health claims (reduction of disease risk)

**Note under the EU Regulation this category of claims also includes; (i) psychological and behavioural functions; (ii) slimming or weight-control or a reduction in the sense of hunger or an increase in the sense of satiety or to the reduction of the available energy from the diet.*

The European Regulation (as do most regulations and the Codex Guidelines) requires scientific substantiation to support any claim. The second European Commission Concerted Action lead by ILSI Europe was the Process for the Assessment of Scientific Support for Claims on Foods (PASSCLAIM), which was completed in March 2005 (Asp et al 2003, 2004; Aggett et al 2005). The final consensus document of PASSCLAIM (Aggett et al 2005) reflects the work of more than 150 scientists from around the world and delivers criteria to assess the scientific evidence to support claims on foods. It is a consensus document that has been the subject of wide and intensive consultation among diverse stakeholders including academic experts, representatives of public interest groups, regulators and the food industry. If met, these criteria provide a reasonable assurance that scientific data underpinning health claims made for foods are adequate for the purpose and that the claims can be considered valid. The publication also discusses the relative strengths and limitations of types of scientific approaches and data that are relevant to different health and disease states as well as providing guidance on the interpretation of the criteria.

FUFOSE and PASSCLAIM have had a considerable impact both within the European Union and at Codex. The PASSCLAIM criteria provide a scientific framework to facilitate assessment of health claims and assure consumers that claims are based on well founded and justified data. They also provide the agri-food industry with a stable framework within which to develop new products with benefits for health and well-being.

- ILSI’s work was referred to in 12 presentations at an EFSA (European Food Safety Authority) Conference on Nutrition and Health Claims in November 2006 (EFSA 2006).
- At the same conference, most speakers on the topic of scientific substantiation of health claims alluded to many of the concepts included in PASSCLAIM such as the “totality of evidence”.
- The European Commission has cited PASSCLAIM in its comments to Codex on the substantiation of health claims.

The EU Regulation (EU 2006) states that in relation to health claims on foods “... general principles applicable to all claims made on foods should be established in order to ensure a high level of consumer protection, give the consumer the necessary information to make choices in full knowledge of the facts, as well as creating equal conditions of competition for the food industry”¹. The proposal lays down strict conditions for the use of claims, in particular in Article 4 of the Regulation, which includes the principle that the use of claims is conditional on respecting the overall nutrient profiling of the food.

The Regulation requires that in developing a nutrient profiling system for foods or certain categories of food the following points should be taken into account:

- The quantities of certain nutrients and other substances contained in the food, such as fat, saturated fatty acids, trans-fatty-acids, dietary fibres, sugars and salt/sodium;
- The role and importance of the food (or of categories of foods) in the diet of the population in general or, as appropriate, of certain at-risk groups including children;
- The overall nutritional composition of the food and the presence of nutrients that have been scientifically recognised as having an effect on health.

Various nutrient profiling schemes have been developed to classify healthy or less healthy foods based on their nutritional characteristics. The purpose of these schemes is to help reduce the consumption of foods that may “encourage consumers to make choices which directly influence their total intake of individual nutrients or other substances in a way which would run counter to scientific advice”.

An ILSI Europe Workshop “Nutritional Characterisation of Foods: Science-based Approach to Nutrient Profiling“ was held from 25-27 April 2006 to discuss among the different stakeholders such as government, industry, consumers and academia the various aspects of nutrient profiling schemes (Asp et al 2007).

The Workshop was not intended to reach consensus at the meeting, but rather to review and discuss the different stakeholders’ views. However, the workshop reached a degree of agreement on several central points. Most participants favoured a food category approach rather than an ‘across the board’ system. Most also felt that nutrient profiling schemes should focus on disqualifying nutrients, while taking into due account relevant qualifying nutrients. Levels of each nutrient should be clearly defined for all food categories to be profiled. Reference amounts selected for further considerations were: (1) per 100 g/100 ml, (2) legislated reference amounts and (3) per 100 kcal.

The majority of workshop participants agreed that nutrient profiling schemes should allow for a two-step decision process. In practice this would mean that where a nutrient-based scoring system is used as a first step, a nutrient threshold approach would be applied as the second step in order to manage the different categories of food products.

The Nutritional Characteristics of Foods Expert Group also explored a new approach to assessing the effectiveness of nutrient profiling models using a food based approach (data from five national surveys in EU member states) and statistical quantitative assessment. Foods that were positively or negatively related to a “healthy diet” (Eurodiet 2001) were

¹ Whereas (9) of the Regulation

identified and the ability of a number of different nutrient profiling schemes to identify these indicator foods was assessed. In general, the nutrient profiling schemes that were evaluated were able to identify correctly about 7 such foods out of 10.

All participants agreed that before implementation of nutrient profiling, it is crucial that as far as possible an objective validation should be conducted; including determination of sensitivity and specificity using “indicator foods” selected on their potential to affect major health issues. The management of any adopted system needs to allow it to be dynamic over time and to allow for revision the system when new scientific knowledge emerges.

A summary report and three scientific articles were published as a supplement to the *European Journal of Nutrition* (Asp et al 2007). The titles of the three articles are: 1) Nutrient profiling schemes - overview and comparative analysis 2) A new reference method for the validation of profiling schemes using dietary surveys, and 3) Comparison of different nutrient profiling schemes to a new reference method using dietary surveys.

3.2.3. North America

In the USA, the US Department of Agriculture regulates food commodities such as meat and milk and the Food and Drug Administration (FDA) regulates processed foods under the Federal Food, Drug and Cosmetic Act. Medicine (drugs), food, dietary supplement, food for special dietary use or medical food are all subject to separate rules, and while a formal regulatory system specific for functional foods does not yet exist, it is currently being considered.

The rules around health claims are complex and are summarised in Table 3. The US Congress defined health claims made on foods in the Nutrition Labelling and Education Act (NLEA 1990) as a claim on the label or in the labelling of a food that characterises a relationship between a “nutrient” in that food and a disease or health related condition. These claims must reach the standard of “Significant Scientific Agreement”. A 1997 amendment to the NLEA (Food and Drug Administration Modernization Act (FDAMA)) permits a manufacturer of foods (not dietary supplements) to rely upon a health claim or statement from an “authoritative” scientific body of the United States Government or the National Academy of Sciences (NAS). In a further development in July 2003 (Better Nutrition Information for Consumer Health Initiative), FDA issued documents laying out the criteria by which it would evaluate “Qualified Health Claims” that do not meet the standard of “significant scientific agreement”. Pre-market approval or notification is required for all health claims and the wording for both the claim and for any required “qualification” is prescribed.

For the separate legal category of dietary supplements the Dietary Supplement Health and Education Act 1994 (DSHEA) governs not only the basic definition and safety standards for dietary supplements but also what structure-function claims are permitted. Structure-function claims on foods are not subject to pre-market approval but must not be misleading.

During 2007, the Centre for Food Safety and Nutrition (CFSAN) of the FDA consulted on draft guidance on an Evidence-Based Review System for the Scientific Evaluation of Health Claims (FDA 2007).

Table 3. USA Structure Function and Health Claims

INTENDED USE	REGULATORY STATUS	MARKET ENTRY REQUIREMENTS	DATA REQUIREMENTS
Effect on “structure” or “function” of body	Food	None	Substantiation adequate to make truthful, non-misleading claims
Effect on “structure” or “function” of body	Dietary Supplement (DSHEA)	Simultaneous marketing and notification of FDA re: claim; Use of “FDA disclaimer”	Substantiation adequate to make truthful, non-misleading claims
Health Claim: relationship between a dietary substance and a disease or health condition	Food (NLEA) Dietary Supplement (DSHEA)	Pre-market approval required	“Significant scientific agreement” based on “well designed studies”
Health Claim: relationship between a dietary substance and a disease or health condition	Food (FDAMA)	Notification (FDA can reject within 120 days)	Scientific statement by authoritative US Government or NAS body
“Qualified” Health Claim	Food, Dietary Supplement	Pre-market approval required Use of qualifier or disclaimer	Categories: <ul style="list-style-type: none"> • “good,” but not conclusive evidence • limited and not conclusive evidence • little evidence

See: <http://www.cfsan.fda.gov/~dms/lab-hlth.html>

In Canada, the recognition of the health effects of various food components has sparked legislative interest in functional foods. Foods containing the beneficial ingredients, whether naturally occurring, or as a result of the addition of an isolated component, are termed "functional foods". The proposed Health Canada definition of a functional food is as follows: "similar in appearance to, or may be, a conventional food, is consumed as part of a usual diet, and is demonstrated to have physiological benefits and/or reduce the risk of chronic disease beyond basic nutritional functions". The 2002 amendments to the *Food and Drug Regulations* allow diet-related health claims on foods for the first time in Canada. Five generic claims were approved based on sound scientific evidence that has established a relationship between certain elements of healthy diets and reduction of risk of certain diseases. Guidance is provided for the preparation of dossiers. Nutrient function (biological role) claims are also permitted but are not subject to pre-market approval. (See Canada at the end of the Reference Section).

The terms "functional foods" or "functional ingredient" have arisen from a general belief in the health benefits of certain foods and although it has no legal meaning, it signifies an appreciation that some foods may confer health benefits. While the term "functional foods" is not yet defined in law, ILSI North America defines it as: "Foods that by virtue of physiologically active food components provide health benefits beyond basic nutrition" (Milner 2002). The primary determinant of the regulatory status of these foods is thus their intended use.

ILSI North America (NA) was one of the first of the ILSI branches to look in detail at the science base for health claims by supporting a paper "A Proposal for the Establishment of Scientific Criteria for Health Claims for Functional Foods (Clydesdale 1997). The paper addresses many of the still current issues such as the boundary between food and medicine, definitions and the type and quality of studies needed to validate claims. They went on to examine the challenges in evaluating the risk-benefit of increased intakes of food components that have the potential to provide significant health benefits (Clydesdale 1999).

3.2.4. Latin America

Latin American consumers are, in general, unfamiliar with functional foods, although there are an increasing number of health-conscious consumers in the more urbanized areas who are aware of the importance of diet for health and well-being. In the last few years, a number of new foods that may be considered as functional foods due to their functional or health properties that are acknowledged by health authorities have appeared on the market in some countries. These include a wide variety of foods such as spreads and milk containing phytosterols; milk containing long chain polyunsaturated fatty acids; milk and products with added oligofructose; margarine and yoghurt with fibre; cookies formulated to have low glycaemic index; milk fermented with selected *Lactobacillus* and *Bifidobacterium* strains; products containing soybean proteins and isoflavones; low-cholesterol eggs; and energy and isotonic drinks containing caffeine and other herbal extracts. A number of products in pharmaceutical forms are also included, e.g. fibre-containing products, anti-oxidants and oils containing freeze-dried vegetable/fruit extracts.

In Latin America and the Caribbean, regulations concerning functional and health claims differ from country to country. There is no official or legal definition of functional foods, or specific regulations for functional foods/ingredients. In Brazil, despite the absence of a legal definition, the norms in relation to functional foods were based on the idea of a food (not being a drug) that is part of a normal diet and that can produce benefits beyond basic nutrition. Legislation requires demonstration of the safety and efficacy of novel foods and foods/ingredients that have a claim on the label. All of these products have to be registered and approved by health authorities.

Brazil is also the only country to have well-defined regulations for functional and health claims for either nutrient or non-nutrient components. In almost all other countries such claims are neither prohibited nor regulated. In general, basic nutrient content/functional claims are allowed and subject to some standards and, in practice, health authorities have allowed product claims on a case-by-case basis in several countries (Lajolo 2002). As a consequence, except for Brazil, there is also a lack of formal criteria for scientific substantiation of claims.

In a continuous and dynamic process of updating the legislation, after five years, the Brazilian regulatory authorities decided to review the previously approved health and functional claims. The basis for the review was the availability of new scientific data and information on the difficulty encountered by consumers in understanding the meaning of the wording used in the labelled claim of some products. Moreover, it was noticed that several claims originally allowed were misused, that is, the statements on the label were far beyond what was approved based on the existing scientific data. The review resulted in various products losing permission to use claims and in the case of others, claims had to be modified. Additionally, a positive list of approved horizontal claims linked to specific substances and probiotics was developed and has to be used whenever a product containing the functional ingredient makes a claim. No change in the wording of the approved claim is allowed.

In Argentina the growing market also indicated a need for regulation and a science base for those regulatory controls. ILSI Argentina started to organise conferences in 1998 and more recently has been asked by the regulatory authorities for input on the science base for regulation. ILSI Brazil has been active since 2000 and is working closely with the Brazilian Agency of Health Surveillance (ANVISA)/ Ministry of Health in order to contribute to the advance of scientific basis for regulating Functional Foods in the country. ILSI Mexico is now interacting with Mexican Government agencies, along with the Codex Alimentarius Commission, as well as many academic and research institutions, trade unions and industrial groups to design a scientific model for health and nutrition claims to be included in food and food products legislation.

Collectively, the Latin American branches of ILSI have set up a group – the Latin America Functional Food and Labelling Network. ILSI Mexico is preparing a summary of the similarities and differences in regulations across the Region as a step in examining the issue of the science base for harmonisation.

3.2.5. Codex Alimentarius

The topic of functional foods was first formally discussed during the 47th Session of the Executive Committee of the Codex Alimentarius Commission in 2001 when the Asian region proposed to commence work in the area of novel foods (other than those derived from biotechnology), functional foods and foods that were also considered to be at the food/drug interface.

In response to the above, the delegation from Malaysia introduced a discussion paper on the subject during the 13th Session of the FAO/WHO Regional Coordinating Committee For Asia Meeting held in Kuala Lumpur, Malaysia in September 2002 (FAO/WHO 2003). The first part of the paper considered the need to define the scope and concept of functional foods, to establish a classification system and criteria for making health claims and to evaluate the safety of functional foods. The second part of the document referred to the need for a clear definition of novel foods (other than from biotechnology) and for a framework for their safety assessment. In order to provide guidance on these issues, the Malaysian delegation recommended the convening of a Joint FAO/WHO Expert Consultation on functional foods and novel foods to examine the need for an international standard to provide better regulatory control of these foods, with the objective of benefiting the global industry and the consumers. Such an Expert Consultation has not been convened thus far although the FAO regional office in Bangkok did organise an expert consultation amongst nutritionists in the Southeast Asian region in November 2004.

These activities have paralleled discussions at Codex in the CCFL (Codex Committee on Food Labelling) and CCNFSDU (Codex Committee on Nutrition and Foods for Special Dietetic Uses) to develop Guidelines for nutrition and health claims (CAC/GL 23-1997, Rev. 1-2004) and on the scientific basis of health claims (still under discussion). ILSI has continued to provide scientific input to these discussions by drawing on the activities of its branches and indeed reference to PASSCLAIM was made by the European Commission in their comments to Codex on the scientific basis for the substantiation of health claims and the PASSCLAIM criteria are included in the drafts considered so far.

3.3 Scientific Advances

In addition to the two international symposia, all ILSI branches have provided opportunities at workshops, seminars and conferences for scientists to share information on the biological effects of functional foods or to examine in detail particular areas of biological function such as antioxidant systems or gastrointestinal microbiology. By bringing together scientists from different groups and backgrounds these events have no doubt stimulated additional research projects. A particularly useful strategy has been to organise a sponsored sessions on specific topics at larger conferences organised nationally or internationally by other groups. This not only is more cost effective but also has the advantage of potentially reaching a wider or new target audience of scientists. ILSI NA has used this approach in organising, each year, in conjunction with the American Society for Nutritional (ASN) a symposium prior to Experimental Biology (EB), an annual event attracting 500 academics and health professionals (see below).

The ILSI NA Technical Committee on Food Components for Health Promotion has a goal to increase the understanding of how specific components in food can improve health and prevent disease. Each year the Technical Committee on Food Components for Health Promotion collaborates with the American Society for Nutrition to organize a special scientific session at Experimental Biology (EB). The special session in 2007 was titled *Functional Foods for Health Promotion: Role of Diet in Affecting Immune System Function*. A number of publications document scientific exchanges in prior years (See EB Annual in the References Section 6 for further information). A notable publication was a supplement of a series of papers on biomarkers based on the 2002 session at EB (Freudenheim 2003). The ILSI NA Project Committee on Flavonoids seeks to expand scientific knowledge and gain consensus concerning the role of dietary flavonoids and health and is supporting an epidemiological study to compare consumption of flavonoids with heart health outcomes.

ILSI Brazil also uses the strategy of organising sessions on specific topics at larger conferences. For example ILSI Brazil sponsored three Symposia on Functional Foods during the Latin American Congress of Nutrition held in Florianópolis, Santa Catarina in November 2006. This is the most important meeting in Latin America in the nutrition field. About 2,000 people attended the Congress with each symposium attracting about 500 attendees. Another example is the “Prize for research on foods with functional properties and bioactive components”. The prize was first awarded by ILSI Brazil in November 2006 and will be awarded every two years. The objective of this initiative is to identify, recognise and encourage new talents in the research area of Functional Foods.

Crucial to the discussion in both FUFUSE and PASSCLAIM and identified by ILSI SEA Region and Australia as a critical issue, is the identification and validation of biomarkers. These are essential where the end health benefit or outcome is not directly measurable. As noted above, ILSI NA has also contributed to the science base on this topic. There was a joint ILSI SEA Region/Australasia meeting in conjunction with Commonwealth Scientific and Ministerial Research Organisation (CSIRO) in Brisbane, 2004. Both PASSCLAIM and the ILSI SEA Region’s 2005 Expert Consultation and 3rd Asian Workshop on Functional Foods have reached consensus amongst the participants on the criteria for biomarkers (see Annex). However, it is likely that debate will continue in this developing field, especially with advances in metabolomics (see Future Directions).

The challenges and promises offered by the merger of ‘biomics’ technologies and mechanistic nutrition research are immense. The ILSI Japan Endowed Chair of Functional Food Science and Nutrigenomics, which is supported by 32 food companies, started in 2004 and taking this opportunity, ILSI Japan organized a “Research Forum on Food Functionality” in 2005 to explore topics related to biomics.

In the same year, the ILSI Europe Nutrition and Genetics Task Force published a review entitled “Nutrigenomics: the impact of biomics technology on nutrition research” (Corthésy-Theulaz et al 2005). This review describes the principles and technologies involved by using nutritional research examples and applications as well as discussing the limitations of genomics, transcriptomics, proteomics, metabolomics and systems biology. In June 2007, a roundtable expert workshop was organised by the Metabolic Imprinting Task Force to discuss the definitions of metabolic imprinting and metabolic programming, which tend to be used interchangeably. “Epigenetic” appears, however, to be a term that is more rigidly defined in terms of specific mechanistic consequences linked to defined clinical outcomes. The

workshop also discussed the use of predictive biomarkers and, in particular, where and which animal models can be used to help develop mechanistic hypotheses that can subsequently be tested in humans. Additionally, biomarkers that are currently used for adults are not (always) appropriate for infants in predicting disorders later in life. Moreover, many of the clinical investigations that can be used in adults cannot be used in infants for ethical or practical reasons. The final paper will be published in the *British Journal of Nutrition* in the second half of 2009.

ILSI branches continually hold conferences, seminars and workshops and support independent reviews on a variety of topics relevant to functional foods science. Reports of some of these activities can be found in the branch links from the ILSI home page <http://www.ilsi.org>.

3.4 Industry Developments

The marked development of functional foods exhibits large regional differences. Asia/Australasia clearly lead the way due to the massive Japanese market for functional foods. The main determinants of market developments include: regulation and legislation, developed market for processed foods, consumer demand for supplementary nutrition, consumer confidence in industry and products, health awareness and perception of novel foods and techniques.

An informal survey of ILSI Europe member companies indicated that ILSI's work on functional foods has benefited them directly. Activities help member companies keep up to date with scientific and regulatory developments in the field and help companies understand the basis of a sound scientific dossier on functional foods and health claims, essential to marketing new products. They believe that promoting the use of the same template by regulators and competitors will aid the harmonisation of rules and lead to smoother approval processes.

Member companies do not mention the theme of Food Technology as a benefit. Few of the ILSI Branches has addressed the topic and none has addressed the topic of product development, taste and consumer expectations. As part of the FUFOSE project, an expert group of ILSI Europe on Food Technology identified three key areas for technological challenges in the future:

1. The creation of new functional food components in traditional and new raw materials and by *de novo* synthesis.
2. The optimisation of functional food components in raw materials and in foods (e.g. maximal preservation or retention of components, modification of their function and their increased bioavailability).
3. The effective monitoring of the amount and efficacy of functional food components in raw materials and in foods.

A separate publication (Knorr et al 1998) documents these key areas in detail using a number of examples to illustrate the variety of challenges: microbial technology, bioactive proteins, minerals, carbohydrates and antioxidants. However, the topic was inevitably not given as much attention as the scientific basis of claims that formed the core of the programme and publications.

3.5. Consumer Aspects

Until recently, the topic of consumer understanding and perceptions about functional foods and health claims had not been addressed in depth. One publication from ILSI Europe – a Concise Monograph on Concepts of Functional Foods (Ashwell 2002) provides information accessible to scientists and non-scientists with an interest in the field. This Concise Monograph is also available in Spanish. An additional Concise Monograph on Functional foods From Science to Health and Claims was published in 2008 and introduces to the non-specialist concepts of functional foods including PASSCLAIM results, assessment of food functionality, the role of functional foods and new technologies, public health aspects, communication and consumer science issues (Howlett 2008). The monograph helps the reader gain insight into the dynamic area of functional foods and their potential for nutrition science and public health. However, ILSI has recognised the importance of Consumer Sciences and several branches (including ILSI SEA Region, ILSI Europe and ILSI Argentina) are currently implementing activities in the field (see Future Directions).

ILSI SEA Region worked with the Asia Food Information Council to conduct a consumer survey on perception of nutrition and health claims in 2006. The preliminary results indicated that consumers related functional foods to short-term health impacts. Respondents did not draw a distinct line between essential nutrients and other functional bio-actives, both the categories being perceived as “good for health”.

Health claims should assist consumers to make informed choices as well as help them identify particular foods and food components with health benefits. In the framework of the proposed new EU regulation on nutrition and health related claims, the ILSI Europe Consumer Science Task Force set up an expert group activity and prepared a scientific article that summarises many of the scientific approaches and decision making frameworks that could be used to provide and assess the evidence of consumers’ understanding of health claims to support submissions for new claims. It specifically considers methodologies that can be developed to assess how consumers are able to verbalise what the health claim is and what the food or food component does.

The aim of the expert group’s paper that was published in the *British Journal of Nutrition* (Leathwood et al 2007a) was to focus on the definition and measurement of correct consumer understanding of health claims. It includes:

- A review of key ideas in the new EU legislation and an elaboration on the regulatory definition of “consumer understanding”;
- An exploration of consumer understanding of health claims from the viewpoint of consumer information processing;
- A presentation of the different research methodologies that provide different sources of evidence to substantiate consumer understanding (qualitative approaches, quantitative surveys and questionnaires, heuristics, purchase and consumption data). It is the first attempt to consider these four methodologies to assess consumer understanding of health claims.

The paper was the basis for an ILSI Europe workshop on Consumer Understanding of Health Claims in May 2006 to stimulate the debate on how nutrition and health claims can exert effects on consumer behaviour and, in particular, to consider methodologies that can be developed to assess how consumers understand health claims. The summary report of the workshop was published in 2007 in the *ILSI Europe Report Series* (Leathwood et al 2007b). Key outcomes were to recommend appropriate methodological approaches to demonstrate adequate consumer understanding proportionate to the nature of the claim and to identify further gaps and research needs. The Report also summarises the general conclusions that were reached by the workshop participants and highlights some areas that would benefit from further discussion regarding the application of some aspects of the legislation.

4. A NEW PERSPECTIVE ON FUNCTIONAL FOODS

The science of “functional foods” encompasses numerous different themes beginning with the origin of the food, including the process by which it was produced, the active component in the food, the assessment of the physiological consequences of its intake, the scientific basis for assessment and regulation through to understanding the perceptions and behaviour of the consumer.

The ILSI Europe Functional Foods Task Force has proposed a way of clustering these items as follows (see Figure 1):

“Technology” is the first cluster. This deals with food technology from the farm to the plate, including plant breeding and biotechnology. Technology is also applied to steps that provide appropriate storage, processing, food enrichment and fortification as well as enhanced taste and function. These are all important steps to ensure the composition, quality and safety of the food.

Functional benefits in foods or drinks in the diet may be provided by the total diet, by a specific food, by an ingredient or by a food supplement. Increasingly it is the individual components of foods that are of interest in the development of functional foods.

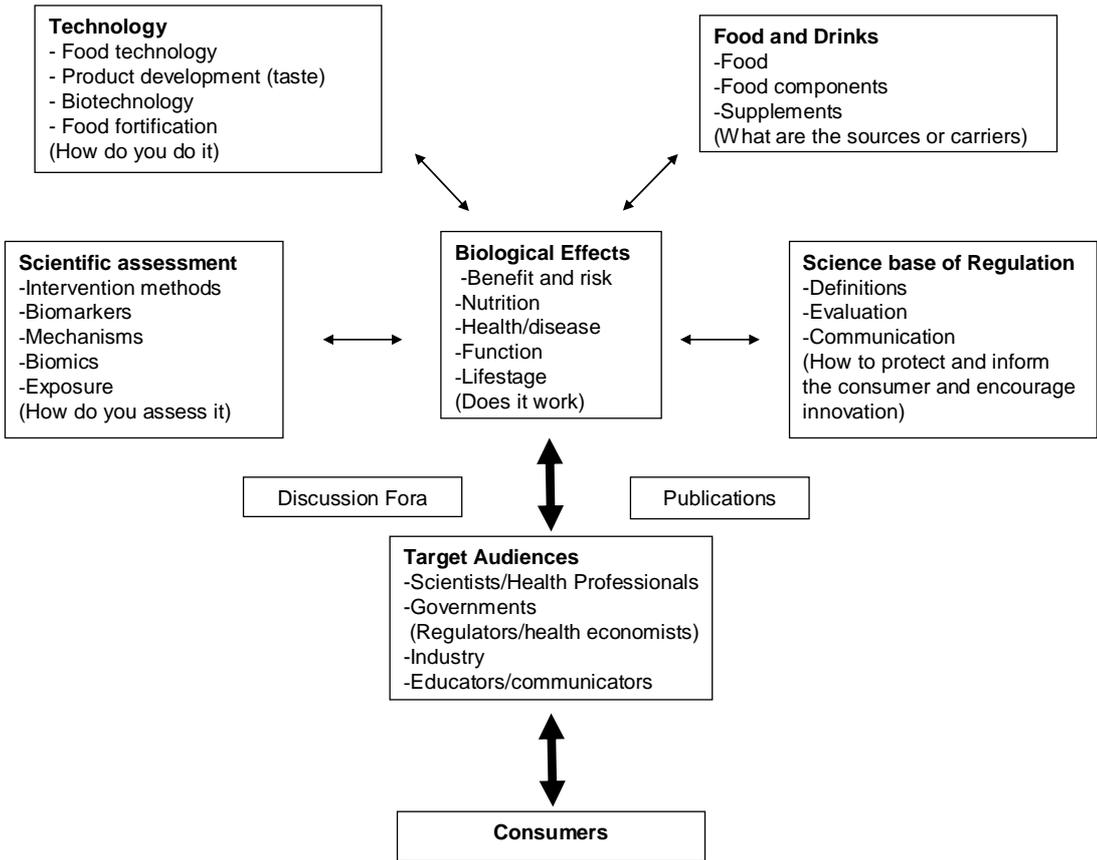
Every functional food is identified by a biological effect(s) on the host. Therefore, biological assessment of the effect of the functional food is essential. It does not matter whether that effect is on the physiology, the psychology, or on the physio-pathology of the consumer, whether that effect is considered as a normal nutritional effect or one beyond traditional nutrition. It must be emphasised that the boundaries of nutrition are moving and will evolve with the progress of science.

The scientific assessment of the food and its effect is a key issue for ILSI because it is one of the major scientific issues where consensus and progress in knowledge are necessary. Here is where the importance of biomarkers comes to the forefront, as it is not always possible to measure the health outcome or endpoint. Understanding the mechanism of the biological effect, while not essential, can also be a useful tool in assessing the impact of the functional food. Better methodology is needed in these fields.

The science base of regulation remains an important topic with links to all of the above: we need to understand what science is required from the four clusters above to underpin the regulations in terms of definitions, evaluation of safety and assessment of claims.

Furthermore, for all this information to reach and be understood by the target audiences additional inputs are required. Understanding the economics of health care could help ILSI provide relevant information to those concerned about improving health care and reducing costs. On the consumer side, while ILSI does not produce information targeted directly to consumers, the social and behavioural sciences help us understand the perceptions and influences that drive peoples’ food choices and related lifestyle behaviours and how best to communicate to the consumer.

Figure 1: A New Perspective on Functional Foods



5. FUTURE DIRECTIONS AND RECOMMENDATIONS

There are a number of challenges to be tackled by ILSI in its future work on functional foods. It is necessary for ILSI to consider these in the context of the wide breadth of this field and to prioritise its objectives and activities appropriately.

- Functional food science is a complex field and it would be misleading to believe that all scientific aspects are covered by the clusters in the scheme above (Figure 1).
- The whole field cannot be addressed by ILSI task forces and scientific committees that are specifically focused on functional foods.
- Some activities will be best left to other groups. It will also be necessary for ILSI FTF to collaborate with other task forces as well as with external scientific groups (e.g. learned societies and scientific trade groups) in order to meet its objectives.
- Nations and also ILSI branches are at different stages of development in terms of the functional food market and the regulatory framework.
- There are some gaps in ILSI's activities to date, notably in the fields of food technology and consumer science although steps are being taken to address the latter.

5.1 Key Priorities for Global Action

A discussion was held at the ILSI branch meeting in January 2007. There were 25 attendees representing 8 branches (NA, Mexico, N Andean, Europe, India, SE Asia, Japan, and Focal Point China). Many of the topics described in the sections below were considered and four priorities were identified for action globally:

- Global harmonisation of scientific substantiation of health claims – scientific input to Codex
- Bio-markers/components/clinical studies database
- Applying the PASSCLAIM and ILSI SEA Region criteria to the assessment of foods or food components
- Consumer understanding of health claims

Note that ILSI Europe and ILSI SEA Region remain the key branches where interest and action in functional foods and health claims is the highest. However, as a priority, it is recommended that each branch appoint a Functional Food Co-ordinator.

5.1.1 Global harmonisation for substantiation

There is no doubt that ILSI has provided a truly international platform for discussion, debate and consensus and that ILSI's inputs and outputs have been relevant, timely and of high quality. However, it remains true that there is a lack of global consensus on the definition and classification of functional foods as well as of nutrition and health claims. This is largely due to a difference in philosophy about the role of functional foods (for example the classical Descartes' principle of one cause, one effect and the Eastern understanding where balances between sets of causes generating cascades of consequences). Whereas the logical approach of the West might be expected to lead to a more pragmatic approach, in fact the tensions that

exist worldwide between scientific progress and consumer protection mean some innovative thinking is needed to make progress.

However, there should be room for global consensus on the scientific substantiation of health claims. The EU now has harmonised legislation, and guidance on the scientific substantiation of health claims from the European Food Safety Authority (EFSA 2007). While North America and Australia/New Zealand also have their own approaches, ILSI SEA Region continues to discuss harmonisation of approaches while Latin America is probably dependent on the outcome of Codex deliberations.

Recommended Action:

- ILSI should continue to provide scientific input and the branches are committed to making a single, global ILSI input available to Codex as their deliberations continue.
- ILSI should consider providing a simplified summary of the full PASSCLAIM Consensus Criteria report that provides more information than the simple list of criteria.
- In countries or regions where the interest in the science base for regulation is just emerging PASSCLAIM/ILSI SEA Region criteria should be put forward by ILSI branches.

5.1.2 Science Base of Regulation in Practice

ILSI Europe is working on a project to apply and test the PASSCLAIM criteria on polyphenols, a broad group of plant components with many putative health benefits.

As a follow up to PASSCLAIM, ILSI Europe is also working on a project to provide best practice advice on the conduct of human trials. Different approaches are required for trials on functional effects and disease risk reduction than for those conducted on medicines so new parameters may need to be defined. Furthermore, there is a need for discussion on what level of evidence will be acceptable for substantiation of health claims. Will it be necessary to have absolutely definitive evidence and complete scientific consensus (even for well established diet-disease relationships there are studies that are not consistent) or could there be a category for, say, ‘highly probable’ substantiation.

The results of many human investigations outside the USA are not being captured in available clinical databases. This is often a waste of valuable resources and reduces the opportunities for standardisation and for comparison between studies.

Recommended Action

- The ILSI Europe project to apply PASSCLAIM criteria to polyphenols should be broadened to a joint project with ILSI SEA Region.
- See also item 5.1.3 on a database for biomarkers.
- ILSI branches could collaborate to provide a forum for a discussion about levels of evidence and how to develop a consistent approach to evaluation of the evidence on the health benefits foods and food components.

- ILSI could encourage investigators to share their experimental protocols with others by adding information in available USA databases, including PDQ (Physician Data Query) if the focus is cancer (<http://www.cancer.gov/cancertopics/pdq/cancerdatabase>), or, for more global human studies, the Clinical Trials database (<http://clinicaltrials.gov>).

5.1.3 Scientific Assessment - Biomarkers

Biomarkers were clearly agreed upon as a priority as they are very often essential for demonstrating biological effect. Biomarkers range from those for exposure to those used for surrogate disease endpoints. The laboratory development of biomarkers is clearly beyond the scope of ILSI FTF but documenting the developing science and dissemination of up to date information are predecessors to the acceptance of new biomarkers. There are also thousands of food components on which the available data are growing.

Biomarkers are essential for the study of many functional foods. For example, it is unlikely we could measure myocardial infarction (heart attack) as an endpoint in a study on food. However, it is possible to measure intermediate end points such as changes in serum cholesterol or in *intima media* thickness (a measure of artery narrowing). These can act as markers for coronary artery disease and hence risk of a heart attack. Following the work of ILSI NA (Freudenheim 2003) there are numerous areas to consider for future progress of biomarkers including:

- Biomarkers for the measurement of exposure – for example there is no biomarker for exposure to dietary energy.
- Biomarkers of health rather than of pathological conditions. For example, polyps, gut enzymes, gut metabolites or measures of DNA damage may all act as signals for the presence of intestinal tract cancers (Rafter et al 2004 – see in Asp et al 2004). It is unlikely, however, that these markers can be used to describe enhanced health.
- For certain functions it may be difficult to demonstrate a benefit for a function that applies to extreme conditions. For example, the benefits of daily training are not easy to measure in the steady state but can be easily demonstrated during a short run or a standardised test. Therefore, physiological challenge-tests and relevant markers must be determined and agreed upon.
- Consumers are not all the same. They need and may expect different kind of benefits. For example, the growing individual is building bone mass while the ageing individual is losing bone mass. Determining the appropriate biomarkers for skeletal health and function will be critical to assessing the value of a functional food for different target audiences.
- Healthy aging may depend on small changes in diet over a long period of time. Surrogate markers for disease risk, but also for health maintenance must be validated to be able to measure a small daily benefit: this will require a dramatic improvement in the precision and accuracy of physiological measurements. For example, insulin sensitivity can be measured accurately by the gold standard methods such as the euglycaemic clamp, but simple, rapid measures are not yet available for screening the impact of interventions.

Recommended Actions

- There is an opportunity to develop, using modern computing technology, a database to document foods and food components together with analytical methods, relevant biomarkers of exposure and effect, methodology for biomarker measurement and references to clinical and other studies that support (or do not support) that there is a biological effect.
- ILSI FFTF should continue the work started in PASSCLAIM and promote the development of biomarkers essential to the development of functional foods by conducting expert, critical reviews of emerging biomarkers and concluding what markers are sufficiently validated and what gaps should be addressed.
- ILSI could foster collaboration around the world to encourage harmonised methodologies and standards. ILSI North America should follow developments at NIH and other government agencies, as they are responsible for the validation of markers in the USA and those that FDA recognises as surrogate markers of risk or disease outcomes.
- FFTF should also ensure that its target audiences, including regulators and, indirectly, consumers are kept informed of developments.

5.1.4 Consumer Understanding of Health Claims

While ILSI does not target the consumer directly with its publications, a better understanding of consumer science is of great importance. Currently, consumer science is of most interest to ILSI SE Asia and ILSI Europe and some activities have already started. Although consumer understanding will inevitably have important cultural dimensions, the purpose of this initiative is to develop a scientific basis for the measurement of consumer understanding that will transcend such differences.

Many consumers are paying more attention to health issues and trying to improve their well-being by changing their diet. However, this increased attention to health and dietary issues is in direct contrast to the increasing prevalence of obesity throughout the globe indicating a widening gap between information and knowledge on the one hand and behaviour on the other hand. Furthermore, many consumers are reluctant to trade taste and convenience for health benefits (Health Focus 2005).

For consumers to accept functional foods, the market must demonstrate trust and credibility and the products' efficacy. Communicating scientific evidence to consumers has proven to be very difficult. Yet consumer understanding is a requirement of the new EU Regulation on Health Claims.

Studies have shown that consumers in different countries perceive claims differently (van Trijp and van der Lans 2007, Bech-Larsen and Grunert, 2003). For example, US consumers generally appear to perceive products with claims regarding disease reduction as being healthier than products bearing physiological claims, whereas European consumers do not seem to differentiate significantly between the two. It seems that the consumer perception of claims crucially depends on whether or not consumers are familiar with the specific (combination of) words that are being used in the claim.

The acceptance and understanding of the concept of functional foods is also affected by customs and cultural habits. For instance, in Europe and Japan products targeting digestive problems such as probiotics are more prevalent, while in the United States these products are not as popular probably due to not having the same tradition of consuming fermented dairy products. Instead, fortified products tackling specific problems such as stress, fatigue and depression as well as bone-health related problems seem more successful on the American market.

ILSI Europe held a workshop in May 2006 and provided input (Leathwood et al 2007, 2007a) to ILSI SEA for their conference in July 2007. ILSI SEA is also collaborating with the Asian Food Information Council (AFIC) in a Consumer Survey on Understanding of Functional Foods. The International Food Information Council (IFIC) and the European Food Information Council (EUFIC) as well as many government and academic groups have also studied the topic. There is probably a need for some consistency of approach in order to make surveys comparable.

Another aspect of some future functional foods that consumers should be willing to consider is new technology – be that genetic modification of plant foods or the application of nanotechnology. An insight into consumer understanding of benefit-risk – something they need to understand to benefit from functional foods – will also help communication about safe, new technologies.

Recommended Action

- Understanding what consumers understand and what motivates them is key to improving food choice behaviour and thus dietary intakes. It is also critical for the food industry to understand motivation to purchase their products. Developing consistent, science based methodology would be of interest to policy makers and industry alike.
- Continued collaboration should be planned and implemented between the two lead branches ILSI Europe and ILSI SEA Region together with IFIC, AFIC and EUFIC as well as academic and even government groups.
- The communication of risk and benefit is critical to functional foods, particularly those based on new technology. Once the ILSI Europe task force has completed its activities on benefit-risk analysis in the BRAFO project (see Section 5.2.5) the next steps could be to examine what implications this has for the education of and communication to the consumer.
- ILSI FTF could take on the challenge of integrating the sciences of physiology (including taste), psychology and sociology and the way they interact to determine consumer behaviour. This would provide insights that will not only help the food industry to develop the right products but will also provide insights for those wishing to develop food policy and at a practical level provide dietary advice to the individual.

5.1.5 Integration

As noted above, functional food science is a complex field and it would be misleading to believe that all possible scientific aspects can be addressed by ILSI FFTF. It will therefore be necessary for them to collaborate with other task forces as well as with external scientific groups (Learned Societies and Scientific Trade groups) in order to meet its objectives and to assist the integration of disciplines such as nutrition, biomedics/biophysics, food technology/bioengineering and consumer science.

There is a need for a much more proactive and consistent flow of relevant, considered information and also the co-ordination of collaborative activities.

Recommended Action

If ILSI wishes to maintain Functional Foods as a global priority then each ILSI branch should appoint a Functional Food Co-ordinator who is responsible for:

- i) Monitoring the activities of all other task forces and keeping the FFTF informed of relevant proposals and activities so that the FFTF may make inputs and become involved as appropriate.
- ii) Keeping FFTF aware of relevant outputs from other task forces.
- iii) Maintaining an awareness of external activities on functional foods.
- iv) Reporting all the above to the global network to an agreed time-frame (e.g. 6 monthly) bearing in mind a fast track route should be open to notify the network of urgent items.

5.2 Other Opportunities

ILSI Europe and ILSI SEA Region are the branches most active on functional foods and ILSI Europe is already exploring some of these topics in task forces other than FFTF. The topics are presented according to the scheme in Figure 1 and not in order of priority.

5.2.1 Food Technology

The production technology for a “functional food” spans existing and future knowledge: it could be a traditional food including the preservation of the desired “effect” along the food chain, or it could be the result of a specific design of process, adapted biotechnology, the addition of an ingredient, the concentration of a natural ingredient or based on other technological know-how. It has been a tradition for food processors to mimic what was once made in the home and we are still discovering that some traditions have a scientific basis.

The application of science to cultivation, harvesting, animal husbandry and food storage is the first step of the food technology chain. For example, modern biotechnology has application in plant and animal breeding. Where a plant is grown can affect the level of micronutrients such as selenium that are dependent on soil composition. The amount of vitamin C in an orange increases during maturation but the impact of refrigerated storage will differ from that of “storage” on the tree. The maturation of a fruit might be a key factor for the ability to provide some specific phytochemicals so the specification of the species, the cultivar and the storage of a plant may become a key part of the specification of the food.

The first challenge for the food technologist, after making a food edible and enjoyable, is to protect the nutritional qualities of the food. Both classical and new processes can and will help to protect compounds lost during traditional processing: a common example is the destruction of heat sensitive compounds during thermal processing. New technologies such as nanotechnology may for example find application in order to incorporate certain unstable bio-active compounds into foods.

Identification and understanding of the exact mechanism of action of the food or the food component, will help to define the core parameters that the process must either generate or protect in order to maintain the efficacy of the food. For example, olive oil was first of interest for its mono-unsaturated fats but now scientists are interested in its various phytochemicals. At each step progress in technology must be able to ensure the production of a given food with appropriate qualities and specifications. Another important challenge for the processor may be to provide a defined absorbability taking into account also that the food matrix may impact the release of a bio-active compound.

Finally, but not least, food technology will have to provide the usual expected benefits for the consumer: taste and pleasure, convenience and shelf life as well as safety. Consumers will not eat foods that do not meet these expectations.

New technology will also no doubt find application in the development of functional foods. For example nano-encapsulation may be used to deliver certain oil-soluble components into a water-based product. Biomolecular technology as well as allowing us to predict health outcomes may be used to help the food technologist.

Recommended Actions:

ILSI is not, as noted above, very active in the field of food technology as applied to product development so in the context of functional foods ILSI FFTF should look for opportunities to ally with other relevant ILSI task forces and/or other external groups such as Food Science and Technology groups such as The International Union of Food Science and Technology (IUFOST)

5.2.2 Foods and Drinks – Understanding Plant Components

It has been estimated that about 25,000 different chemical compounds occur in fruits, vegetables and other plants eaten by man. Some of those compounds that have received much attention and which show potential to influence a variety of cellular processes that would be expected to influence health include carotenoids, dithiolthiones, flavonoids, glucosinolates, isothiocyanates, allyl sulfhydryls and fermentable fibres (Milner 2002).

Nevertheless, dietary guidance to consume diets rich in fruits and vegetables as well as whole grain remains based primarily on observational studies and on traditional use apart from a broader body of evidence on dietary fibre. The focus has been on “antioxidant” components of plants and until recently the additional evidence base consists of animal studies, *in vitro* and *ex vivo* studies. Intervention studies have been combined with *ex vivo* techniques (for example Dragsted et al 2006) but these are still only possible biomarkers of the risks of disease end points that we are really interested in such as CVD and cancer.

There is a great need to understand better the protective effects of plant foods in order to guide the future directions for plant breeding, product innovation as well as public health advice. We also need much more information about food composition. Recently the USDA has compiled a database of flavonoid content of a range of foods together with an appraisal of the quality of the compositional data (USDA 2006). However, the task of analysing and compiling all relevant compositional data is daunting. It is also interesting that a recent report commissioned by FAO (2007) has recommended the development of an international database of biologically active components from plants, animals and micro-organisms.

Co-ordination across branches and task forces will be paramount to achieve progress in this field. The amount of information that is made available each year on this topic is overwhelming and there is a great need for a critical appraisal of this in order to keep target audiences informed of real progress and relevant, key developments.

In order to test and refine the PASSCLAIM criteria, ILSI Europe is supporting a project to apply the criteria to the assessment of polyphenols as noted in section 5.1.2. The project also (i) includes an attempt to assess the amount of intake of polyphenols required to exert claimed effects (and this can also link to the benefit-risk project below) and (ii) attempts to identify *in vitro* techniques that could be used to screen polyphenols.

Recommended Actions

- ILSI Europe should liaise with ILSI NA Flavonoid Committee to determine what completed projects might inform the European work
- ILSI may be able to make use of the extensive USDA work on the flavonoid content of certain foodstuffs (USDA 2006)
- The recommended action under 5.1.3 to use “smart” Information Technology to develop a database on biomarkers can be logically extended to document data on plant components. This should be of interest to ILSI Europe, ILSI SEA Region and ILSI Japan (for their work on teas). Ultimately, this would have worldwide application and support might be gained from FAO.

5.2.3 Scientific Assessment - Biomics

With the rapid advances in our understanding of nutrigenomics (the impact of our genes on our biological responses) and nutrigenetics (the effect of nutrients on gene expression) and the potential for the application of metabolomics, it is essential to assess the impact of these findings on the science-base of functional foods, particularly as it relates to scientific assessment.

As noted in Section 3.3, the importance of biomics technology on nutrition research has already been recognised by ILSI in the endowment of a Chair of Functional Food Science and Nutrigenomics in Japan, in the organisation of a conference in Singapore (Tai 2007) and in a European publication (Corthésy-Theulaz et al 2005). Externally, the need for international collaboration to agree harmonised and standardised methodology has been highlighted in recent publications (e.g. Gibney et al 2005).

Recommended Actions

- ILSI could seek opportunities to co-ordinate international groups in their collaborations or ILSI Europe could collaborate to submit project proposals under the European Commission Seventh Framework Programme.
- ILSI Europe and ILSI Japan should consider a workshop on metabolomics in the next five-year plan.

5.2.4 Scientific Assessment – Intake Exposure

ILSI task forces have contributed a great deal to the topic of exposure to (intake of) food components such as food additives and flavours. There may be synergies for the ILSI FFTF with these other activities. For example, the ILSI Europe Addition of Nutrients to Food Task Force is assessing the pattern of intake of fortified foods and food supplements on the basis of existing food intake databases. There may be synergies in methodology that could be applied to assessment of exposure to other groups of foods.

In addition the ILSI Europe Novel Foods Task Force published a paper on “post-market monitoring” (PMM) which is “a means to confirm that the actual intakes are within the expected range of intake and that there are no unexpected effects when a large population including diseased people and those of a diverse genetic makeup are exposed for potentially long periods of time” (Hepburn et al 2008). PMM does not replace appropriate pre-market risk assessment.

Recommended Actions

- Functional Food Co-ordinators to exchange relevant updates.

5.2.5 Biological Effects - Benefit-Risk Evaluation

A functional food is a food with a benefit (or a biological effect) beyond basic nutrition that is communicated to consumers by translating it into a function or health claim. The benefit may be to enhance a function or to reduce the risk of a disease. The benefit may occur only at a certain time of life (window for activity) or only in specific population group depending on differences in physiology.

Foods are not pharmaceuticals that are taken by a specific individual and where risk to that individual can be balanced by a benefit. For functional foods it is important to determine that the benefits for the majority do not carry a risk for other consumers not in the target group. For example, the current debate about whether general fortification of flour with folic acid to prevent neural tube defects might carry an increased risk of cancer development in individuals with precancerous or benign tumours. There may also be considerations of risk in certain genetic subgroups.

Full benefit-risk assessment will require more knowledge of human physiology, of the relevant marker(s) to explore the changes, and specifically to assess the improvement of a function before toxic events become evident, as well as determination of intermediate end-points for various risks of diseases. Assessing the consequences of an improvement of a function may require the definition of the normal (physiological) range of variation, the upper safe limit of improvement, as well as consideration of the impact on metabolic regulatory

systems. Finally, but perhaps most importantly, the benefit and the risk must be expressed with the same unit of measurement in order to be able to calculate the benefit-risk ratio.

In September 2007 ILSI Europe initiated (but not under the FFTF) a Specific Support Action under the EC Sixth Framework Programme to investigate the *Benefit-Risk Analysis of Foods (BRAFO)*. The 3-year project is considering as a starting point the evaluation of changes in the quality/duration of life using a system that allows weighting of data quality and severity of effect. The main objectives of this specific support action are to:

- Establish a common unit of measurement for comparing risks and benefits quantitatively for food and food components present in the diet.
- Provide a scientific framework to aid in the objective comparison of benefits and risks and improve harmonisation of the principles and practices in the benefit-risk analysis process, thereby facilitating decision-making.

Three groups will review the literature to undertake a risk analysis, a benefit assessment, an exposure evaluation and quantitative net health impact assessment on the following selected cases: natural foods (fish and soy selected as examples), dietary interventions (folic acid will be considered for food supplementation, and macronutrient replacers for food substitution) and heat processing of foods.

Recommended Action

- ILSI Europe Functional Foods Co-ordinator to ensure that the global network is kept fully informed of activities, opportunity for inputs and of interim and final outcomes.

5.2.6 Biological Effects – Benefits and Life Stages

Although there have been many meetings and symposia on different topics there is still much work to be done in terms of understanding the biological effects of functional foods so that foods can be identified or formulated for target conditions or life stages not only to reduce disease risk but also to promote health. Some priority areas are:

- i) Mental function - for example improved cognitive performance in children and in older age groups where there may usually be a decline in cognitive function. Addressing diseases such as Alzheimer's and Parkinson's would also be important. Depression, altered mood states etc are also increasing prevalent.
- ii) Wellbeing - a difficult concept; terminology that is widely used by consumers but lacks a science base.
- iii) Weight maintenance/satiety/obesity - there is still a need for effective foods and food components
- iv) Cancer - a difficult area because of a lack of surrogate endpoints
- v) Emerging areas related to CVD such as vascular reactivity

Recommended Action

- ILSI Japan has been active on ageing and its plans to make more information available in English will help share their valuable knowledge.
- ILSI should sponsor systematic reviews of these fields to ensure the best interpretation of the plethora of data

5.2.7 Science Base of Regulation - Nutrient Profiling

In current parlance “nutrient profiling” is the classification of foods for specific purposes based on their nutrient composition. The purpose of nutrient profiling schemes in relation to health claims is to prevent a situation that might “encourage consumers to make choices which directly influence their total intake of individual nutrients or other substances in a way which would run counter to scientific advice” (EU 2006). The concern is largely driven by concerns about obesity and, to a lesser extent, concerns about chronic disease. Various nutrient profiling schemes have been proposed or developed in a wide range of countries in order to classify healthy or less healthy foods based on their nutritional characteristics. However, it is of paramount importance that such schemes are science based and have a common science base around the world – even if schemes have to be adapted to take into account local needs and customs.

ILSI Europe organised a discussion on this topic at an April 2006 workshop (Asp et al 2007) (see 3.3.2) but further work is required.

Recommended Actions

- It is important that the work initiated by ILSI Europe is extended to further validate the food-based approach. The Functional Foods Co-ordinator should keep all branches informed.

5.2.8 Target Audiences - Scientists

ILSI and its branches communicate regularly with its core target audiences increasingly via the Internet – the ILSI newsletter is transmitted electronically by email and this tendency is increasing. For example, ILSI Argentina has recently launched their bimonthly Newsletter aimed at medical doctors, nutritionists, regulatory and health authorities as well as the industry. ILSI Europe and ILSI NA are responsible for most of the peer-reviewed publications leaving an opportunity for other branches to follow suit.

Workshops and conferences provide an opportunity for essential face-to-face contact where real progress can be made, especially when consensus is sought. There have been some key initiatives and events that are well documented especially in SEA Region and Europe. However, many of these projects and events remain poorly documented and unfortunately few publications have emerged. Publications are also the means by which information is brought to a larger, broader or even a new target audience. Therefore, it is important for all ILSI branches to examine what events should lead to formal publications, preferably peer-reviewed, over and above branch or international newsletters.

Scientists in industry, academia and government, as well as regulators and health professionals and other interested parties can access the scientific publications that all ILSI branches produce. However, ILSI should assess the value of these publications to each of the target audiences so they can be better tailored to suit their needs.

There may be new target audiences such as health economists that ILSI should consider reaching. The increasing costs are a burden on health care systems around the world. Most healthcare systems depend for their direction on fairly short-term principles based on acute

treatment and waiting lists. Preventative medicine has a long history and is probably best developed in the East where a more holistic and balanced approach was taken to an individual's health. In the Western world health budgets rarely provide much resource to preventive measures and where these are put into place, the focus is often on thresholds for drug treatment rather than diet. Furthermore, general dietary intervention has in practice proved relatively ineffective whereas simple interventions with functional foods may, theoretically, offer cost effective results. For example, there has been an analysis of the potential population benefits of the use of phytosterol-fortified margarine in Germany (Gerber et al 2006).

Recommended Actions

- All ILSI FFTF should always consider publication and should find cost effective ways to disseminate information more widely and effectively for example on the Internet.
- ILSI should also consider ways to determine the value of their activities and publications to their target audiences. Simple surveys are an obvious route but may provide inadequate information because the response rate to surveys is often poor. Other means of obtaining the information could be based on validated market research methods.
- ILSI FFTF could evaluate opportunities to work on the cost/benefit aspects of functional foods to provide valuable input to those developing health policies.

6. REFERENCES

Note: www links correct as at February 2009

Aggett PJ, Antoine J-M, Asp N.G. et al. (Guest eds) (2005). Process for the Assessment of Scientific Support for Claims on Foods (PASSCLAIM) – Consensus on Criteria. *European Journal of Nutrition* 2005; 44(1): 1-30.

Ashwell M. Concepts of Functional Foods (2001). *ILSI Europe Concise Monograph Series*.

Asp NG, Cummings JH, Mensink RP, Prentice A, Richardson DP (2003). Process for the Assessment of Scientific Support for Claims on Foods (PASSCLAIM) – Phase One: Preparing the Way. *European Journal of Nutrition* 42(Suppl 1): 1-119

Asp NG, Cummings JH, Howlett J, Rafter J, Riccardi G, Westenhoefer J (2004). Process for the Assessment of Scientific Support for Claims on Foods (PASSCLAIM) – Phase Two: moving forward. *European Journal of Nutrition* 43(Suppl 2): 1-183.

Asp NG, Drewnowski A, Flynn A and Przyrembel H (eds) (2007). Nutritional Characterisation of Foods: Science-based Approach to Nutrient Profiling. *European Journal of Nutrition* 46 (Suppl 2): 3-46.

Bech-Larsen T and Grunert KG 2003 The perceived healthiness of functional foods. A conjoint study of Danish, Finnish and American consumers' perception of functional foods. *Appetite* 40: 9-14.

Bellisle F, Diplock AT, Hornstra G, Koletzko B, Roberfroid M, Salminen S, Saris WHM (1998). Functional Food Science in Europe. *British Journal of Nutrition* 80(Suppl 1): 1-193

Binns N and Howlett J (2008). Functional Foods in Europe - International Developments in Science and Health Claims
<http://europe.ilsa.org/publications/Report+Series/FFsymporeport2008.htm>

Clydesdale FM (1997). A Proposal for the Establishment of Scientific Criteria for Health Claims for Functional Foods. *Nutrition Reviews* 55: 413-422.

Clydesdale F (ed) (1999). Safety assessment and potential health benefits of food components based on selected scientific criteria. ILSI North America Technical Committee on Food Components for Health Promotion. *Critical Reviews in Food Science and Nutrition*, 39: 203-316

Corthésy-Theulaz I, den Dunnen JT, Ferré P, Geurts JMW, Müller M, van Belzen N and van Ommen B (2005). Nutrigenomics: the impact of biomics technology on Nutrition Research. *Annals of Nutrition and Metabolism* 49: 355-365

Diplock AT, Aggett PJ, Ashwell M, Bornet, F, Fern EB, Roberfroid MB (1999). Scientific Concepts of Functional Foods in Europe: Consensus Document. *British Journal of Nutrition* 81: S1-S27

Dragsted LO, Krath B, Ravn-Haren GR, Vogel UB, Vinggaard AM, Jensen PB, Rasmussen SE, Sandstrom B and Pedersen A (2006). Biological effects of fruit and vegetables. *Proc Nutr Soc* 65: 61-67.

EB (Experimental Biology) USA (annual)

http://www.ilsina.org/programs/food_components_health_promotion.htm

EFSA (2006). European Food Safety Authority. Bologna Workshop on Nutrition and Health Claims

http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1178621460354.htm

EFSA (2007) European Food Safety Authority. Final scientific and technical guidance for applicants for preparation and presentation of the application for authorisation of a health claim

http://www.efsa.europa.eu/EFSA/ScientificPanels/NDA/efsa_locale-1178620753812_Guidance467.htm

EU (2006). REGULATION (EC) No 1924/2006 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 20 December 2006 on nutrition and health claims made on foods. *Official Journal of the European Union* 18 January 2007 L 12/3-18.

Eurodiet (2006). Core Report. Nutrition and diet for lifestyles in Europe: science and policy implications. *Public Health Nutrition* 4: 265-273.

FAO/WHO (2003) Discussion paper on functional foods and novel foods (other than from biotechnology). In: *Report of the thirteenth session of the FAO/WHO regional co-ordinating committee for Asia, Kuala Lumpur, Malaysia 17-20 September 2002*. FAO Rome.

FAO (2007). Food and Agriculture Organisation Report on Functional Foods.

FDA (2007). Food and Drug Administration. Evidence-Based Review System for the Scientific Evaluation of Health Claims <http://www.cfsan.fda.gov/~dms/hclmgui5.html>

Freudenheim J (ed) (2003). Biomarkers of Nutritional Exposure and Nutritional Status. *Journal of Nutrition* 133: 871S-973S.

Gerber A, Evers T, Haverkamp H and Lauterbach KW (2006). Cost benefit analysis of a plant sterol containing low-fat margarine for cholesterol reduction. *The European Journal of Health Economics*. Published online 5 July. 10.1007/s10198-006-0363-0

Gibney MJ, Walsh M, Brennan L, Roche HM, German B and van Ommen B (2005). Metabolomics in human nutrition: opportunities and challenges. *Am J Clin Nutr* 82: 497-503

Hepburn P, Howlett J, Boeing H, Cockburn A, Constable A, Davi A, de Jong N, Moseley B, Oberdörfer R, Robertson C, Wal JM, Samuels F (2008). The Application of Post-Market Monitoring to Novel Foods. *Food and Chemical Toxicology* 46: 9-33

- Howlett J. Functional Foods – From Science to Health and Claims (2008). *ILSI Europe Concise Monograph Series*.
- Knorr D et al. (1998) Functional Food Science in Europe. *Trends in Food Science and Technology* 9: 293-344
- Lajolo, FM. Functional foods: Latin American perspectives (2002). *British Journal of Nutrition* 88 (S2): 145-150.
- Leathwood P, Richardson DP, Sträter P, Todd P and van Trijp H (2007a). Consumer Understanding of Nutrition and Health Claims: Sources of Evidence. *British Journal of Nutrition* 2007; 98(3): 474-484.
- Leathwood P, MacFie H and van Trijp.H (2007b). Consumer Understanding of Health Claims. *ILSI Europe Report Series*: 1-23.
- Madsen C. Functional Foods in Europe: International Developments in Science and Health Claims. *Ann Nutr Metab* 2007;51:298–299
- Milner JA (2002). Functional foods and Health: A US perspective. *Brit J Nutr* 88: (Suppl 2) 151-158
- Nutrition Reviews (1996). The First International Conference on East-West Perspectives on Functional Foods. *Nutrition Reviews* 54: (11) (part II) S1-S202
- Saris W et al (2002). International Symposium on Functional Foods: Scientific and Global Perspectives *British Journal of Nutrition* 88[S2]: S123-S235.
- Tai ES, Gillies PJ (eds) (2007): Nutrigenomics – Opportunities in Asia. *Forum Nutr*. Basel, Karger, 60:1-248
- Tee ES (2003). Report of ILSI Southeast Asia Region Coordinated Survey of Functional Foods in Asia. ILSI Southeast Asia Region, Singapore.
- Tee ES (2004). Functional Foods in Asia – Current Status and Issues. ILSI Southeast Asia Region, Monograph Series, Singapore.
- Tee ES (2007). Development of Approaches and Guidelines for Functional Foods in Asia. <http://europe.ilsa.org/NR/rdonlyres/C7E7AD1A-60CC-49CF-8EC1-C58CB7B6DE00/0/ILSISEAposter07final.pdf>
- van Trijp HCM and van der Lans IA (2007). Consumer perceptions of nutrition and health claims. *Appetite* 48: 305–324
- Verschuren P 2002. Symposium Report on Functional Foods – Scientific and Global Perspectives. *ILSI Europe Report Series*.

USDA (2006) United States Department of Agriculture Database for the Flavonoid Content of Selected Foods. Release 2

<http://www.nal.usda.gov/fnic/foodcomp/Data/Flav/Flav02.pdf>

WHO (2004). Global strategy on diet, physical activity and health. The Fifty-seventh World Health Assembly, Resolution Number WHA57.17.

References to International Approaches to Regulate Health Claims (Table 1) - correct at April 2009

Australia/New Zealand - Food Standards Australia/New Zealand (Draft)

<http://www.foodstandards.gov.au/foodmatters/healthnutritionandrelatedclaims/>

Brasil - Ministério da Saúde. Agência Nacional de Vigilância Sanitária. List of approved claims:

http://www.anvisa.gov.br/alimentos/comissoes/tecno_lista_alega.htm.

Canada – Health Canada

<http://www.inspection.gc.ca/english/fssa/labeti/guide/tab8e.shtml>

Codex Alimentarius - ALINORM 08/31/26 Codex Committee on Nutrition and Foods for Special Dietary Uses Session 29. Paragraphs 79 – 97.

<http://www.codexalimentarius.net/web/archives.jsp?lang=en>

and

Guidelines for nutrition and health claims (CAC/GL 23-1997, Rev. 1-2004).

EU REGULATION (EC) No 1924/2006 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 20 December 2006 on nutrition and health claims made on foods.

http://eur-lex.europa.eu/LexUriServ/site/en/oj/2007/l_012/l_01220070118en00030018.pdf

Japan – Ministry of Health, Labour and Welfare

<http://www.mhlw.go.jp/english/topics/foodsafety/fhc/02.html>

USA – Food and Drug Administration. Center fo Food Safety and Applied Nutrition

<http://www.cfsan.fda.gov/~dms/lab-hlth.html>

ANNEX

**Guidelines and Criteria for the substantiation of claims
A comparison with PASSCLAIM and Codex and ILSI SEA Region**

	PASSCLAIM ¹	Proposed Draft Codex Recommendation ²	ILSI SEA Region Final Guidelines ³
1. Characteristics of food for which a claim is to be made	The food or food component to which the claimed effect is attributed should be characterized.	<p>“Property of a food” includes energy, nutrients, biologically active substances or components, ingredients etc. May also be applied to whole diet</p> <p>Adequate characterisation (para 4.3.1)</p>	Characteristics of functional foods are as given in ILSI SEA Region Monograph on Functional Foods and subsequently revised at their Expert Consultation on Functional Foods from December 5-6 2005
2. Types of studies or scope of evidence required for substantiation of claims	Substantiation of a claim should be based on human data, primarily from intervention studies,	<p>All health claims should be based on well designed human interventions (clinical) studies. Animal model studies and <i>in vitro</i> studies may be provided as supporting knowledge – not enough per se to substantiate</p> <p>SPECIAL CASES</p> <ul style="list-style-type: none"> • Health claims bearing on fully recognised functions of nutrients and for which reports on clinical studies have been 	<ul style="list-style-type: none"> • Nutrient function claims** may be permitted based on authoritative statements from recognized health authorities and accepted texts. • Scientific substantiation of other function claims** should be based on human data (observational and/or intervention studies). <i>In vitro</i> studies and animal studies may be submitted in

	PASSCLAIM ¹	Proposed Draft Codex Recommendation ²	ILSI SEA Region Final Guidelines ³
		<p>published in the scientific literature</p> <ul style="list-style-type: none"> • The totality of the evidence may only comprise observational evidence particularly for health claims involving a diet/food group/whole food • Nutrient function claims may be substantiated based on generally accepted authoritative information that has been verified and validated over time. • In order to substantiate a ‘reduction of disease risk’ claim, which offers the highest ‘degree of promise’, a rigorous step-by-step evaluation of the available evidence should be required according to the outline given [in the Codex Guidelines] 	<p>support of the application.</p> <ul style="list-style-type: none"> • Disease-risk reduction** claims would require additional data from randomized double-blind placebo controlled trials (RCT). In the event that this is not possible, data from appropriately designed intervention studies can be accepted. <p>** <i>Definition of claims are based on definition of Codex Health Claims (FAO/WHO, 2004) :</i></p>

	PASSCLAIM¹	Proposed Draft Codex Recommendation²	ILSI SEA Region Final Guidelines³
4. Research design and methodology	<p>The design of studies should include the following considerations:</p> <ol style="list-style-type: none"> 1. Study groups that are representative of the target group 2. Appropriate control 3. An adequate duration of exposure and follow up to demonstrate the intended effect 4. Characterization of the study group's background diet and other relevant aspects of lifestyle 5. An amount of the food or food component consistent with its intended pattern of consumption 6. The effect of the food matrix and dietary context on the functional effect of the component 7. Monitoring of compliance with intake of food or food component under test 	<p>The scientific evidence should:</p> <ul style="list-style-type: none"> • provide adequate characterization of the property of the food • ensure that study groups are representative of the target group. • characterise the target groups' background diet and other relevant aspects of lifestyle • [ensure] intake is consistent with its intended pattern of consumption • [ensure] adequate duration of exposure • [consider the] influence of the matrix and dietary context. 	<ul style="list-style-type: none"> • Studies should preferably be conducted on whole functional foods in the form to be consumed rather than on extracted components. • Foods containing added functional food ingredient(s) may not need individual studies to be conducted if they can show bioequivalency compared to the primary study conducted. • Study group should be relevant to the intended claim and target population. When the target population is different from the subjects of the original studies, the application has to justify the product is still effective and safe. • Appropriate control is required.

	PASSCLAIM¹	Proposed Draft Recommendation²	Codex	ILSI SEA Region Final Guidelines³
				<ul style="list-style-type: none"> • Adequate length of duration of exposure and follow-up to demonstrate the intended effect is needed. • Dietary intake of human subjects should be characterized and monitored as part of the intervention studies and should be conducted using appropriate methodologies. • Compliance of consumption of food or ingredient under investigation should be monitored. • An amount of food or dose of food component used should be consistent with its intended pattern of consumption. • The effect of the food matrix and dietary context on the functional effect of the component should be

	PASSCLAIM ¹	Proposed Draft Recommendation ²	Codex	ILSI SEA Region Final Guidelines ³
				<p>considered.</p> <ul style="list-style-type: none"> • Studies should be conducted using methodologies accepted by the scientific community. • Studies should have been approved by the appropriate ethical committee. • Study must include adequate number of subjects to reach confident conclusions.
Statistical methods	<ul style="list-style-type: none"> • The statistical power to test the hypothesis [should be considered] • Within a study, the target variable should change in a statistically significant way and the change should be biologically meaningful for the target group consistent with the claims to be supported. 			<ul style="list-style-type: none"> • Statistical power to test the hypothesis and clinical meaningfulness should be considered. • Statistical analysis of the data shall be conducted with methods recognized as appropriate for such studies. • Statistical, biological and clinical significance should be used for proper

	PASSCLAIM¹	Proposed Draft Recommendation²	Codex	ILSI SEA Region Final Guidelines³
				interpretation of the research.
3. Biomarkers	<p>When the true endpoint of a claimed benefit cannot be measured directly, studies should use markers.</p> <ul style="list-style-type: none"> • Markers should be: <ul style="list-style-type: none"> • Biologically valid in that they have a known relationship to the final outcome and their variability within the target population is known • Methodologically valid with respect to their analytical characteristics 	<p>In the step by step process there is the following statement:</p> <ul style="list-style-type: none"> • Identify the proposed relationship between the food property, and the health endpoint for a health claim. • Identify appropriate measurements for the property and the health endpoint. 		<ul style="list-style-type: none"> • The claimed functional benefit should be measured directly if possible. In situations when this is not possible, appropriate biomarker(s) as intermediate endpoints, should be identified and used in the studies. • A relevant biomarker is a well-defined biological, physiological, clinical or epidemiological indicator which is modulated by the ingestion of the food, food constituent or ingredient and for which there is agreement among the scientific community on the relation between the modulation of this indicator and the state of health of the population in which it is measured.

	PASSCLAIM¹	Proposed Draft Recommendation²	Codex	ILSI SEA Region Final Guidelines³
				<ul style="list-style-type: none"> • In disease risk reduction claims, the biomarker(s) considered should be a marker(s) of that disease and recognized by the scientific community. The change of the level of such a biomarker(s) would significantly affect the risk of disease or health condition which is the substance of the claim (Guidelines from WHO Technical Report Series 916 may be referred to). • Suitability of a given biomarker(s) within a population or between population groups should be assessed, based on variability of response. • Methodology for measuring the biomarker(s) should be generally accepted by the international scientific community relative to that

	PASSCLAIM ¹	Proposed Draft Codex Recommendation ²	ILSI SEA Region Final Guidelines ³
			discipline.
5. Evaluation based on totality of data	A claim should be scientifically substantiated by taking into account the totality of the available data and by weighing of the evidence.	<ul style="list-style-type: none"> The totality of the evidence should be reviewed – supporting, contradicting and ambiguous evidence Evidence based on human studies should demonstrate a consistent association between the property and health effect, with little or no evidence to the contrary. <p>STEP BY STEP PROCESS</p> <p>Typically includes:</p> <ol style="list-style-type: none"> Identify the standard of evidence for substantiation and other policies for health claims. Identify the proposed relationship between the food property, and the health endpoint for a health claim. Identify appropriate measurements for the property and the health endpoint. Identify and categorise all the evidence. Assess and interpret the 	<ul style="list-style-type: none"> All available positive and negative outcomes must be taken into account by a group of qualified experts, based on a clearly described search strategy. Studies should be peer-reviewed and preferably be published in scientific journals. Studies conducted by independent research groups are preferred. Studies conducted by or funded by industry may be acceptable on condition that the research is independently peer reviewed. The body of research shall convincingly demonstrate that the product will have the claimed effect at the

	PASSCLAIM ¹	Proposed Draft Codex Recommendation ²	ILSI SEA Region Final Guidelines ³
		evidence, study-by-study. 6. Evaluate the totality of the evidence across studies and determining if, and under what circumstances, a claimed relationship is substantiated.	recommended level of intake.
6. Safety		<p>Specific safety concerns:</p> <ul style="list-style-type: none"> • When the claim is about a food constituent, the amount should not expose the consumer to health risks and the known interactions between the constituent and other constituents should be considered. • The expected level of consumption shall not exceed any relevant upper level of intake for food constituents. • The exposure assessment should be based on an evaluation of the distribution of usual total daily intakes for the general population and, where relevant, those for vulnerable 	

	PASSCLAIM ¹	Proposed Draft Recommendation ²	Codex	ILSI SEA Region Final Guidelines ³
		<p>population groups.</p> <ul style="list-style-type: none"> • It should account for the possibility of cumulative intake, when the same constituent is present in several foods, and for nutritional imbalance due to changes in dietary patterns in response to consumers' information laying emphasis on the food property. 		
7. Re-evaluation		<p>Health claims should be re-evaluated, after a certain period of time (possibly every 5-10 years) or following the emergence of significant new evidence. Health claims should be re-evaluated only if new evidence calls into question the scientific validity underpinning the claim.</p>		<p>Re-evaluation will be based on the proper assessment of significant new findings</p>

1. P Aggett, J Antoine, N-G Asp, L Contor, J Cummings, J. Howlett, D. Muller, C Persin, L Pijls, G. Rechkemmer, S Tuijelaars, H Verhagen. PASSCLAIM (Process for the assessment of scientific support for claims on foods); Consensus on Criteria. Eur J Nutr (2005), Suppl 1, 44: p 6.
2. FAO/WHO (June 2006). Proposed draft recommendations on the scientific basis of health claims at step 3. CX/NFSDU 06/28/7
3. Developed at ILSI SEA Region's Expert Consultation on Functional Foods, December 5-6, 2005, Singapore & 3rd Asia Region Workshop, July 18, Malaysi

