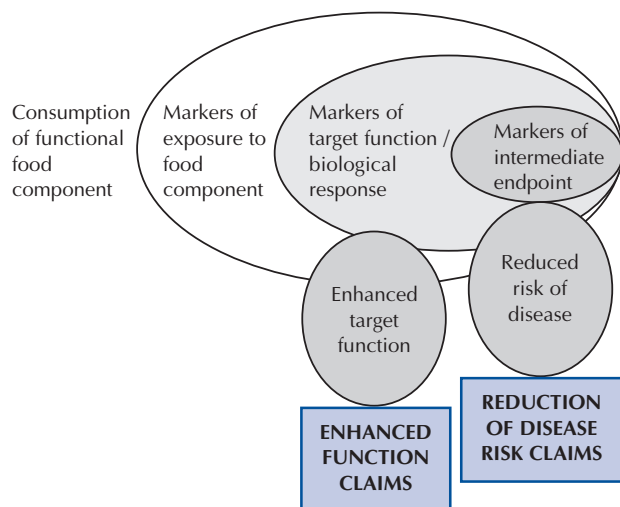


A proposal for a scientific basis for claims



# CONCEPTS OF FUNCTIONAL FOODS

ILSI



International  
Life Sciences  
INSTITUTE

## **ABOUT ILSI / ILSI EUROPE**

The International Life Sciences Institute (ILSI) is a nonprofit, 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.

This publication is made possible by support of the ILSI Europe Functional Food Task Force, which is under the umbrella of the Board of Directors of ILSI Europe. ILSI policy mandates that the ILSI and ILSI branch Boards of Directors must be composed of at least 50% public sector scientists; the remaining directors represent ILSI's member companies. Listed hereunder are the ILSI Europe Board of Directors and the ILSI Europe Functional Food Task Force members.

### ***ILSI Europe Board of Directors members***

Prof. N.-G. Asp, Swedish Nutrition Foundation (S)  
Prof. B. Beaufrère<sup>†</sup>, Université d'Auvergne (F)  
Prof. P.A. Biacs, Bay Zoltán Foundation for Applied Research (H)  
Prof. J.W. Bridges, University of Surrey (UK)  
Prof. G. Eisenbrand, University of Kaiserslautern (D)  
Prof. M.J. Gibney, University of Dublin (IRL)  
Dr. M. Horisberger, Nestec Ltd. (CH)  
Dr. M.E. Knowles, Coca-Cola West Europe (B)  
Dr. I. Knudsen, Danish Veterinary and Food Administration (DK)  
Prof. R. Kroes, IRAS – Utrecht University (NL)

Dr. G. Malgarini, Ferrero Group (B)  
Mr. J.W. Mason, Frito Lay Europe (UK)  
Ir. J.-F. Molle, Groupe Danone (F)  
Dr. D.J.G. Müller, Procter & Gamble European Service GmbH (D)  
Prof. L. Serra Majem, University of Las Palmas de Gran Canaria (E)  
Drs. P.J. Sträter, Südzucker AG Mannheim/Ochsenfurt (D)  
Prof. V. Tutelyan, National Nutrition Institute (RUS)  
Prof. W.M.J. van Gelder, Royal Numico (NL)  
Drs. P.M. Verschuren, Unilever Health Institute (NL)  
Dr. J. Wills, Masterfoods (UK)

### ***ILSI Europe Functional Food Task Force member companies***

Barilla Alimentare S.p.a.  
BASF Aktiengesellschaft  
Cerestar R& D Centre  
Coca-Cola Eurasia & Middle East  
Colloïdes Naturels International  
Danisco Sweeteners  
Danone Vitapole  
Döhler Group  
DSM Food Specialties  
Ferrero Group  
GlaxoSmithKline  
Kellogg's Company of Great Britain Ltd.  
Masterfoods  
Nestec Ltd.

Numico Research  
Nutrinova  
Parmalat  
Procordia – Orkla Foods  
Procter & Gamble European Service GmbH  
Puleva Biotech S.A.  
Raffinerie Tirlémontoise – Orafti  
Roche Vitamins Europe Ltd.  
Rudolf Wild GmbH & Co. KG  
SQTS – Swiss Quality Testing Services  
Südzucker AG  
Valio Ltd.  
VK Mühlen AG  
Yakult UK Ltd.

# CONCEPTS OF FUNCTIONAL FOODS

By Margaret Ashwell



**ILSI Europe**

© 2002 International Life Sciences Institute

*All rights reserved.* No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording, or otherwise, without the prior written permission of the copyright holder. The International Life Sciences Institute (ILSI) does not claim copyright on U.S. government information.

Authorization to photocopy items for internal or personal use is granted by ILSI for libraries and other users registered with the Copyright Clearance Center (CCC) Transactional Reporting Services, provided that \$0.50 per page per copy is paid directly to CCC, 222 Rosewood Drive, Danvers, MA 01923. Phone: (+1) 978 750 8400, Fax: (+1) 978 750 4470.

ILSI®, “A Global Partnership for a Safer, Healthier World.®”, and the International Life Sciences Institute (ILSI) logo image of the microscope over the globe are registered trademarks of the International Life Sciences Institute. The use of trade names and commercial sources in this document is for purposes of identification only and does not imply endorsement by ILSI. In addition, the views expressed herein are those of the individual authors and/or their organizations, and do not necessarily reflect those of ILSI.

For more information about ILS/ILSI Europe, please contact

ILSI Press  
One Thomas Circle, NW  
Ninth Floor  
Washington DC 20005-5802  
USA  
Phone: (+1) 202 659 0074  
Fax: (+1) 202 659 3859  
E-mail: [ilsipress@ilsi.org](mailto:ilsipress@ilsi.org)  
Website: <http://www.ilsi.org>

ILSI Europe  
Avenue E. Mounier 83, Box 6  
B-1200 Brussels  
Belgium  
Phone: (+32) 2 771 00 14  
Fax: (+32) 2 762 00 44  
E-mail: [info@ilsieurope.be](mailto:info@ilsieurope.be)  
Website: <http://europe.ilsi.org>

*Printed in Belgium*

ISBN 1-57881-145-7

# ***CONTENTS***

---

FOREWORD .....	1
INTRODUCTION .....	3
FUNCTIONAL FOODS AND HEALTH .....	6
HOW DOES THE CONSUMER LEARN ABOUT THE HEALTH BENEFITS OF FUNCTIONAL FOODS? .....	16
HOW SHOULD CLAIMS BE SUBSTANTIATED AND APPROVED? .....	20
SOME EXAMPLES OF FUNCTIONAL FOOD COMPONENTS .....	24
TECHNOLOGY IN THE DEVELOPMENT OF FUNCTIONAL FOODS .....	29
FUTURE PERSPECTIVES .....	32
GLOSSARY .....	35
FURTHER READING .....	38

## FOREWORD

---

Balanced diet is a major concept that results from a century of research in nutrition as a consequence of the discovery of nutrients and their requirements for the development, growth and maintenance of the body. It has been the main driving force in support of the elaboration of dietary recommendations and food guidance. But, at the turn of the 21st century, new challenges arise in nutrition science.

The definition of health is no longer restricted to the absence of disease, but it includes physical as well as mental and psychological well-being. Food is not only required for body development, growth and maintenance but it is also recognised to play a key role in the quality of life.

Functional food is a recent concept that originated in Japan but was further developed in the United States and in Europe. This concept implies that foods and food components have the ability to beneficially influence body functions to help improve the state of well-being and health and reduce the risk of diseases.

In the 1990s, ILSI Europe developed a functional food project that was submitted as a European Commission (EC) concerted action. This concerted action, known as FUFOS (Functional Food Science in Europe), started in 1995. Over a period of three years it involved about 100 European experts in nutrition and medicine who critically assessed the state of the art in functional foods. They reviewed the scientific literature about foods and food components and their capacity to modulate body functions. These experts then worked on the concept of functional food and elaborated, for the first time, a global framework that included a strategy for the identification and development of functional foods and for the scientific substantiation of their effects, in order to justify health-related claims. In particular, the experts recommended the use of two types of claims to characterise functional foods: enhanced

function claims and reduction of disease risk claims, which are now under discussion in the expert committees of the Codex Alimentarius. Finally, they produced the “Scientific Concepts of Functional Foods in Europe: Consensus Document”.

The present concise monograph has been based on the work and the documents produced by these experts, and especially the Consensus Document on Scientific Concepts of Functional Foods in Europe and the results of the EC-funded FUFOS concerted action. Functional food is a concept aimed at stimulating research in nutrition to support and validate the development of new foods and food components. It belongs to nutrition, not to pharmacology. Progress is also being made in biomedical research creating new opportunities for development in nutrition science.

As clearly stated in the concise monograph as well as in all the FUFOS documents, functional food is still a scientific challenge, more than a marketing one. The scientific substantiation of claims remains a major objective for the future. It is the topic of a new EC-funded concerted action on the Process for the Assessment of Scientific Support for Claims on Foods, also known as PASSCLAIM.

When validated, these claims will be used to communicate nutritional and health benefits of functional foods to health professionals and consumers. Such a communication is the other major challenge of functional food development for which a multidisciplinary approach is urgently needed.

We are confident that this concise monograph will help readers to gain a short but clear overview of functional foods and we hope that it will establish a sound scientific approach in this fast-evolving area of nutrition and food science.

Anne Franck  
Raffinerie Tirlemontoise - Orafiti

*Author:* Margaret Ashwell

*Scientific Editor:* Marcel Roberfroid

*Scientific Referees:* Christine Williams, Åke Bruce and Berthold Koletzko

*Concise Monograph Series Editor:* Ron Walker

*With special thanks to:* Gayle Crozier-Willi and Fred Brouns

# INTRODUCTION

---

## *Advances in nutrition science*

### **Traditional nutrition**

To appreciate the importance of functional foods, it is helpful to understand how the science of nutrition has changed over the last century. Consuming a nutritionally balanced diet once meant eating an adequate diet to avoid deficiency. But in affluent societies, we have progressed to a stage at which it means consuming an optimal diet for promoting health as well as reducing the risk of diet-related chronic diseases. This exciting development has happened in the following way.

During the first half of the 20th century, nutrition scientists identified the essential nutrients and established nutritional standards, mainly, if not exclusively, with the aim of preventing deficiencies and supporting body growth, maintenance and development. These advances are reflected today in:

- Nutrient reference values, such as the recommended daily allowances (RDAs) or reference nutrition intakes (RNIs), which are “the average daily amounts of essential nutrients estimated, on the basis of available scientific knowledge, to be sufficiently high to meet the physiological needs of nearly all healthy persons”.
- Dietary guidelines that give “advice on consumption of foods or food components for which there is a related public health concern”. These are expressed in relation to total diet, often in qualitative terms (more/less/increased/reduced...), based on consensus research findings relating diet and health.
- Food guides, such as food pyramids or food plates, that are “the translation of nutrition standards and

dietary guidelines in terms of recommendations on daily food intake”. These form a conceptual framework for selecting the kinds and amounts of foods that, together, provide a nutritionally satisfactory diet. They are based on nutrient reference values, composition of foods, food intake patterns and factors influencing food choice.

In the last third of the 20th century, nutritionists also recommended avoiding excessive consumption of certain nutrients after recognising their potential roles in several (mostly chronic) diseases, such as coronary heart disease (CHD), type 2 diabetes, elevated blood pressure and cancer. This led to the recognition that some components of foods, when consumed in sufficient quantities, could have a negative impact on health. Development of a wide range of food products with reduced amounts of certain nutrients, mainly fat, sugar and salt, then followed.

### **Optimal nutrition**

At the turn of the 21st century, the industrialised world faces new challenges, i.e. an enormous increase in the costs of health care, longer life expectancy, improved scientific knowledge, development of new technologies, and major changes in lifestyles. Nutrition scientists want to rise to these new challenges and have embraced the idea of “optimal nutrition”, which focuses on optimising the quality of the daily diet in terms of its content of nutrients and non-nutrients as well as other food properties that favour the maintenance of health. This is where the development of functional foods comes into play.

Achieving optimal nutrition by using functional foods aims at optimising the physiological functions of each of us to ensure maximum well-being, health and quality lifespan. A diet also might have to match our unique biochemical needs. Accordingly, an optimal selection of nutrients in such a diet will rely on a better under-

#### 4 Concise Monograph Series

standing of the interactions among genes, nutritional factors and disease, because these can determine the responsiveness of a specific individual to both the beneficial and adverse effects of his or her diet. These interactions include:

- Genetically determined variations between people in the effects of food components on protective and risk factors for disease.
- Genetically determined interindividual variations between people in the way in which different protective and risk factors can alter the risk of actual disease.

In the future, people may know whether they are at risk for, say, heart disease. They might be able to choose the foods and diets that suit them individually and will have a better understanding of the importance of this personalised selection of foods. This will be a vast improvement over the present situation, in which dietary advice is given to populations in general and individuals are asked to comply with the advice whether it is suited to them or not. Compliance surely will be better with more personalised advice.

#### *Functional foods: defining the concept*

Functional foods cannot be a single, well-defined or well-characterised entity. Indeed, a wide variety of food products are (or in the future will be) characterised as functional foods. These include a variety of components, nutrients and non-nutrients, affecting a range of body functions relevant either to a state of well-being and health and/or to the reduction of risk of a disease. Although many functional food products are in the market, it is easier to explain the scientific rationale behind these foods as a function-driven concept. In this

way, the concept can be universal and not influenced by the local characteristics or cultural traditions that determine the products in specific food markets.

Japan is the birthplace of the term functional food (Box 1). A variety of terms, more or less related to the Japanese Foods for Specified Health Use (FOSHU), have appeared world-wide. These include more exotic terms, such as nutraceuticals, designer foods, f(ph)armafoods, medi-foods, vitafoods and the more traditional dietary supplements and fortified foods. All are foods or food products marketed with the message of a benefit to health.

### **BOX 1**

#### *Functional foods: a Japanese beginning*

In the early 1980s, three large-scale research programmes were launched and funded by the Japanese government on “systematic analysis and development of food functions”, “analysis of physiological regulation of the function of food” and “analysis of functional foods and molecular design”. A category of foods for potential benefits in a national effort to reduce the escalating cost of health care, Foods for Specific Health Use (FOSHU), was established in 1991.

#### **FOSHU**

FOSHU are those foods expected to have a specific health effect as a result of relevant constituents, or those foods from which allergens have been removed.

The effect of such an addition or removal must have been evaluated scientifically, and permission must be granted to make claims regarding the specific beneficial effects on health to be expected from their consumption. To be identified as FOSHU, evidence is required that the final food product, but not isolated individual component(s), is likely to exert a health or physiological effect when consumed as part of an ordinary diet.

FOSHU products should be in the form of ordinary foods (i.e. not pills or capsules).

## **Functional foods: a European consensus**

The EC Concerted Action on Functional Food Science in Europe (FUFOSE) actively involved a large number of the most prominent European experts in nutrition and related sciences and was coordinated by the International Life Science Institute (ILSI Europe). It reached a consensus on “Scientific Concepts of Functional Foods in Europe” in 1999. To reach that final objective, three major steps were taken:

- A critical assessment of the science base required to provide evidence that specific nutrients and food components positively affect target functions (biological responses) in the body.
- An examination of the available science from a function-driven rather than a product-driven perspective.
- An elaboration of a consensus on targeted modifications of food and food constituents and on options for their applications.

Because functional foods is a concept rather than a well-defined group of food products, the FUFOSE Consensus Document proposed a working definition.

A food can be regarded as “functional” if it is satisfactorily demonstrated to affect beneficially one or more target functions in the body, beyond adequate nutritional effects, in a way that is relevant to either an improved state of health and well-being and/or reduction of risk of disease. Functional foods must remain foods, and they must demonstrate their effects in amounts that can normally be expected to be consumed in the diet. They are not pills or capsules, but part of a normal food pattern.

## **TABLE 1**

### **Main points of the working definition for functional foods**

- Food nature of functional food: it is not a pill, a capsule or any form of dietary supplement.
- Demonstration of the effects to the satisfaction of the scientific community.
- Beneficial effects on body functions, beyond adequate nutritional effects, that are relevant to improved state of health and well-being and/or reduction of risk (not prevention) of disease.
- Consumption as part of a normal food pattern.

It was emphasised that a functional food may not necessarily induce a health benefit in all members of the population. Matching selected food component intakes with individual biochemical needs may become a key task as we progress in our understanding of the interactions between genes and diet (Table 1).

From a practical point of view, a functional food can be:

- A natural food in which one of the components has been naturally enhanced through special growing conditions.
- A food to which a component has been added to provide benefits (e.g. the addition of selected probiotic bacteria with proven health benefit characteristics to improve gut health).
- A food from which a component has been removed so that the food has less adverse health effects (e.g. the reduction of saturated fatty acids [SFA]).

## 6 Concise Monograph Series

- A food in which the nature of one or more components has been chemically modified to improve health (e.g. the hydrolysed protein in infant formulas to reduce the likelihood of allergenicity).
- A food in which the bioavailability of one or more components has been increased to provide greater absorption of a beneficial component.
- Any combination of the preceding possibilities.

The rest of this document will consider important issues that relate to concepts of functional foods.

## ***FUNCTIONAL FOODS AND HEALTH***

---

Functional food science is based on the way in which specific nutrients and food components positively affect target functions (biological responses) in the body. In fact, several important areas of human physiology that are relevant to functional food science can be used to illustrate the concept:

- Early development and growth.
- Regulation of basic metabolic processes.
- Defence against oxidative stress.
- Cardiovascular physiology.
- Gastrointestinal physiology.
- Cognitive and mental performance, including mood and alertness.
- Physical performance and fitness.

A short explanation of each is given here, followed by a summary of some potential functional food components that have been or might be developed to improve each relevant health area. This list is not exhaustive, and other areas of physiology, such as “optimal defence against infection”, also have potential for the development functional foods.

A more detailed consideration will be given to the areas of cardiovascular and gastrointestinal (GI) physiology, because most of the current interest in the functional food market, as well as the science that supports functional food products, falls within these areas.

## ***Early development and growth***

The term growth refers to the increase in the number and size of cells of a specific individual and to the changes in body dimensions. Growth is usually associated with increases in length and weight; development indicates the progressive changes that occur in tissues and organs as they gain their specific functions. All mammals start life as a single cell. During the early part of gestation, the fertilised egg divides many times. Different kinds of cells develop during the process of differentiation and then arrange themselves to form the various organs of the body. The general principles of growth apply to all species, but the rate of cell division (the division of the parental cell into a large number of different daughter cells) is genetically determined and depends upon nutrient supply and utilisation. The speed of physical growth is regulated during the life cycle and is controlled by genetics, a variety of growth factors that interact with target cells and environmental factors, including diet.

### **Functional foods to promote optimal development and growth**

The feeding of mothers during pregnancy and lactation and of their infants and young children is of great biological importance. Nutritional factors during early development not only have short-term effects on growth, body composition and body functions but also exert longer-term effects. The development of neural functions and behaviour in adults, as well as overall mortality risks, can be affected by early nutrition – a phenomenon called metabolic programming. The interaction of nutrients and gene expression may form the basis for many of these programming effects and offer exciting potential for functional food development.

The course of pregnancy and childbirth, as well as the composition of breast milk and the short- and long-term development of the child, are influenced by the intake of

nutrients, particularly polyunsaturated fatty acids (PUFA), iron, zinc and iodine.

The evaluation of dietary effects on child growth requires epidemiological and field studies, as well as the evaluation of specific cell and tissue growth. Growth factors and conditionally essential nutrients (e.g. amino acids and PUFAs) may be useful as ingredients in functional foods. Intestinal growth, maturation and adaptation, as well as longer-term function, may be influenced by food ingredients such as oligosaccharides, gangliosides, high-molecular-weight glycoproteins, bile salt-activated lipases, and pre- and probiotics.

Pregnancy and the first postnatal months are critical time periods for the growth and development of the human nervous system, processes for which adequate nutritional supplies are essential. Early diet seems to have long-term effects on sensory and cognitive abilities, as well as behaviour. Possible long-term effects of early exposure to tastes and flavours on later food choice preferences may have a major impact on public health.

Exciting possibilities have been suggested by the beneficial effects of some functional foods on the developing immune response (e.g. the effects of antioxidant vitamins, trace elements, fatty acids, arginine, nucleotides, probiotics and altered allergenic components of infant foods).

Peak bone mass at the end of adolescence can be increased by dietary means. This is expected to be of (long-term) importance for the prevention of osteoporosis in later life. The combined effects of calcium and other constituents of growing bone, such as proteins, phosphorus, magnesium and zinc, as well as vitamins D and K, fluorine and boron, offer many possibilities for the development of functional foods, although many still need to be confirmed by research.

## ***Regulation of basic metabolic processes***

Dietary balance can influence all metabolic and physiological processes. An optimally balanced diet is usually expressed in terms of its energy and content of carbohydrates, fats and proteins. A number of chronic diseases, such as obesity and type 2 diabetes, are partly related to changes in total energy intake, levels of physical activity and poorly balanced diet.

### **Energy balance and obesity**

Obesity is defined as an excessive accumulation of body fat. Its prevalence may vary between 5% and 50% in different populations and also depends on the definition applied. We now recognise the epidemic of obesity with its accompanying health risks to be one of the major health challenges in the developed world. People with central obesity are most at risk. Central obesity appears to be a reflection of increased amounts of internal (as opposed to subcutaneous) fat.

Obesity is associated with an increased risk of heart disease, type 2 diabetes, high blood pressure, and some cancers. The interaction of genetic predisposition and environmental factors, such as a sedentary life style and high-fat diet, is the most commonly accepted model for the cause of human obesity.

### **Diabetes**

Diabetes mellitus is a disease characterised by increased plasma glucose concentrations. Insulin is the hormone that usually controls glucose levels, and diabetes results from impaired insulin secretion or reduced insulin action at its target tissues (insulin resistance).

Two main forms of diabetes mellitus are defined by clinical manifestations and causes. Type 1 or insulin-dependent diabetes usually develops in young, lean individuals and is the result of an almost complete

destruction of the pancreatic beta cells, usually as a consequence of an autoimmune process. Because it is the beta cells that produce insulin, type 1 diabetes is characterised by plasma insulin levels that are very low.

Type 2 or non-insulin-dependent diabetes usually develops in overweight and/or older individuals. It has a very slow onset (the subject may be without clinical symptoms for several years) and is characterised by insulin resistance, resulting in chronically elevated plasma insulin and glucose levels.

### **Insulin resistance syndrome**

Apart from being associated with higher than normal levels of insulin and glucose, insulin resistance is also associated with characteristic changes in lipid metabolism. The lipoproteins are particles composed of specific proteins and lipids (triacylglycerol [TAG], cholesterol and phospholipid) that enable (water-insoluble) lipids to be transported in blood. Low-density lipoproteins (LDL) and very low-density lipoproteins (VLDL) contain high concentrations of TAG and cholesterol, and are termed "low density" on the basis of comparison with the density of water. Elevated levels of LDL and VLDL are recognised risk factors for coronary disease. High-density lipoproteins (HDL) contain low concentrations of cholesterol and are believed to be beneficial. Insulin resistance syndrome may be characterised by increased concentrations of TAG, decreased concentrations of HDL cholesterol and high blood pressure.

## Functional foods for optimising metabolism

This area offers many opportunities for the development of functional foods. The approach to controlling glucose levels is based on choosing foods that cause a slower absorption of glucose into the bloodstream, so that blood glucose fluctuations are less pronounced and, consequently, insulin requirements are lowered. The rate of glucose uptake is influenced by the structural properties of foods, such as the presence of particles, intact cells, starch granules or human-made structures. It is also influenced by certain types of starch and soluble, viscous types of dietary fibre. Organic acids and other components also are known to influence the rate of glucose uptake.

The descriptor “low glycaemic index” is reserved for those foods that are absorbed in the gut but cause only a slow and small rise in blood glucose levels. Examples of such foods are bread with whole grains and/or sour dough, oats, legumes, pasta and products enriched in soluble viscous types of dietary fibre. An increasing body of knowledge is available in this area on which development of functional foods with optimised release of carbohydrates can be based. Already, alternative low-glycaemic ingredients, such as hydrogenated carbohydrates (polyols) or trehalose, are being substituted for high-glycaemic ingredients to improve the glycaemic response to foods.

## *Defence against oxidative stress*

Oxygen is essential to human life. Without it, we cannot survive. Paradoxically, oxygen is also involved in toxic reactions and, therefore, is a constant threat to the well-being of the human body.

Most of the potentially harmful effects of oxygen are believed to be the result of the formation and activity of reactive oxygen species (ROS). These act as oxidants and

are believed to be major contributors to ageing and to many of the diseases associated with ageing, including heart disease, cancer, cataracts, age-related decline in the immune system and degenerative diseases of the nervous system, such as Parkinson’s and Alzheimer’s diseases.

The human body has several mechanisms for defence against ROS. The various defences are complementary to one another, because they act on different oxidants or in different cellular compartments. One important line of defence is a system of antioxidant enzymes. Nutrition plays a key role in maintaining these enzymatic defences. Several essential minerals and trace elements, including selenium, copper, manganese and zinc, are involved in the structure or catalytic activity of these enzymes. If the supply of these is inadequate, enzymatic defences can be poor.

A second line of defence is the group of small-molecular-weight compounds that act as antioxidants, such as glutathione, and some vitamins, like vitamin C or E, that regenerate the buffer capacity of the body’s antioxidant systems.

If exposure to external sources of oxidants is high, the body’s antioxidant defences may be unable to cope. The result is a condition called oxidative stress, an imbalance between pro-oxidants and antioxidants. In the normal situation, pro-oxidant factors are adequately counterbalanced by antioxidant defences. An increase either in the production of oxidants or in a deficiency in the defence system could disturb this balance, causing oxidative stress.

## **Functional foods to promote optimal defence against oxidative stress**

The body's own defences can be supported by a wide variety of small-molecular-weight antioxidants found in the diet, and these give ample scope for functional food components. The best known are vitamin E, vitamin C, carotenoids and polyphenols, including flavonoids. Many of the antioxidant compounds in the diet are of plant origin. Plant leaves are exposed to visible and ultraviolet light and other radiation and are especially susceptible to damage by activated forms of oxygen. Hence, they contain numerous natural antioxidant constituents that can either counter ROS directly or boost the regeneration system to restore antioxidant capacity.

## ***The cardiovascular system***

Cardiovascular diseases (CVD) are a group of degenerative diseases of the entire cardiovascular system and include CHD, peripheral artery disease and stroke.

CHD is a major health problem in most industrial countries. The predominant clinical symptoms are myocardial infarction (heart attack), angina and sudden cardiac death. The arteries supplying blood to the heart are narrowed by atherosclerosis.

To appreciate the role functional foods can play in prevention, it is necessary to understand the many risk factors for CVD. The first group of risk factors include those involved with the integrity of the coronary arteries and other main blood vessels (e.g. control of high blood pressure and control of inflammation). The second group of factors relate to the maintenance of appropriate lipoprotein levels (e.g. LDL cholesterol and insulin resistance), and the third group of factors relate to the likelihood of blood clot formation. The inter-

dependence of all these factors has not been fully characterised. Because only 50% of the incidence of CVD can be explained by known risk factors, other unexplored contributory and interactive factors are probably included. Genetic predispositions also play a major role.

## **High blood pressure**

CVD is directly related to high blood pressure, and any measures taken to reduce high blood pressure should lower the risk of coronary disease. A high blood pressure increases the risk of arterial injury. Genetic predisposition and obesity factors certainly are involved in the aetiology of high blood pressure. However, certain food components (e.g. potassium, calcium and certain fatty acids) may play a major beneficial role.

## **Integrity of artery lining**

Damage to the endothelial cells that line the arteries, as well as more general structural damage at susceptible points in the arteries (such as at "forks"), increases the risk of CVD.

## **Elevated blood lipids**

A raised plasma concentration of LDL is a strong risk factor for CVD. High levels of other lipoproteins, TAG concentrations and low levels of HDL are also risk factors. Raised levels of lipids, especially TAG, after a meal appear to be a stronger risk factor than fasting levels. Long-chain, highly unsaturated, n-3 fatty acids from fish oil may reduce the postprandial TAG response.

## **Oxidised lipids**

Oxidation is now believed to be a major contributor to atherosclerosis, because it converts LDL into an oxidised form. Oxidised LDL has been found in damaged arterial walls and has been shown to have several actions that

could contribute to the initiation and progression of arterial damage. The extent of LDL oxidation is related to the extent of atherosclerosis.

### High homocysteine levels

Epidemiological data suggest that high plasma levels of homocysteine, an amino acid, are associated with increased risk of CVD. Several proposed mechanisms for the effects of homocysteine on atherosclerosis and thrombosis have been suggested, but none has been confirmed.

### Increased blood clot formation

The control of blood clot formation is likely to be an important element in the reduction of the risk of CVD. Risk factors include those that increase the clumping of platelets and those that increase the activity of the clotting factors. These are counterbalanced by factors that promote the breakdown of the clot.

### Low circulating vitamin K

Recent observations indicate that a poor vitamin K status is related to increased calcification of arteries as well as to increased stroke. Vitamin K is involved as a cofactor in the activation of specific proteins that are active in the prevention of calcium deposits in the circulation system. As such, this vitamin contributes to the maintenance of optimal arterial elasticity (arterial compliance). The current recommended levels of intake (based on levels required for optimal blood clotting) may be too low for optimal tissue concentrations.

## Functional foods to promote optimal heart health

### *Balance of dietary lipids*

The levels of blood lipids can be influenced by dietary fatty acids, an influence usually related to their size and shape and the degree of saturation of their hydrocarbon chains.

Fatty acids with a hydrocarbon chain that contains no double bonds are saturated fatty acids (SFAs). SFAs with chain lengths up to 16 carbon atoms increase plasma LDL cholesterol concentrations more than they increase plasma HDL concentrations. In their favour, they cannot be oxidised.

Unsaturated fatty acids are those in which the hydrocarbon chain contains at least one double bond. Monounsaturated fatty acids (MUFA) contain one double bond; PUFAs contain two or more. Most naturally occurring unsaturated fatty acids are *cis* fatty acids, in which the hydrogen bonds are on adjacent sides of double bonds. This causes a bend in the hydrocarbon chain at that point. *Trans* fatty acids have the hydrogen atoms on the same side of the double bond and are straight and more like SFAs. They are formed during some manufacturing processes and therefore consumed in products such as hard margarines and baked goods. About a third of the *trans* fatty acids in the diet come from hydrogenation in ruminants and, consequently, are consumed in dairy products and meat. Dietary *trans* unsaturated fatty acids can increase plasma LDL and reduce HDL cholesterol concentrations. Diets low in SFAs and *trans* fatty acids, therefore, could reduce the risk of CVD.

The *cis*-unsaturated fatty acids with 18 carbon atoms – oleic (monounsaturated), linoleic and alpha linolenic acids (polyunsaturated) – reduce plasma concentrations of LDL cholesterol, and some do this without significantly affecting plasma HDL cholesterol concentrations. Functional foods enriched in these unsaturated fatty acids could also be used to reduce the risk of CVD.

The long-chain, highly PUFAs found in fish oils belong to the n-3 family, which is derived from alpha linolenic acid. They can promote improvements in endothelial and arterial integrity as well as counteract blood clotting. They also reduce plasma TAG and may have suppressive effects on the cellular immune system. One of the focus areas of functional food development concerns the incorporation of n-3 fatty acids into foods.

#### *Other possible functional food components*

Soluble fibre can reduce LDL cholesterol concentrations, particularly in people with high lipoprotein levels.

Diets rich in antioxidants, including plant flavonoids, can inhibit LDL oxidation, influence the activities of immune-competent cells and inhibit the formation of cell-to-cell adhesion factors.

Evidence suggests the possibility of protecting vascular integrity through beneficial modulation of risk factors such as high plasma homocysteine concentrations and high blood pressure. Folate and vitamins B6 and B12 have the potential to reduce cardiovascular risk by lowering the plasma level of homocysteine. An increase in potassium and a reduction in sodium can help to reduce blood pressure (BP).

Two significant areas of functional food development are the use of soy protein and plant sterol and stanol esters to reduce levels of LDL cholesterol (see page 22 for additional details on plant sterols and stanols).

Recent speculation on the role of vitamin K in cardiovascular health indicates a potential role for other, hitherto unsuspected, food components that might significantly affect the development of functional foods for heart health.

## ***Gastrointestinal physiology and function***

The human large intestine (colon) is recognised as one of the most metabolically active organs of the human body. The colon contains an extremely complex microbial ecosystem. In fact, bacterial cells account for around 90% of the total cells in the body. The majority of these bacteria are anaerobic (they die in the presence of oxygen). The most common species in the adult human colon are those of the bacteroides, bifidobacterium and eubacterium.

The infant's colon is sterile at birth, and microflora are acquired during delivery and in subsequent days from the mother and the environment. The initial colonising species create a habitat that is ideal for the growth of strict anaerobes. Thereafter, differences in the composition of the microflora are believed to depend largely on the nature of the diet as well as the host. The microflora of breast-fed infants are dominated by bifidobacteria. In contrast, formula-fed infants have more complex microflora, which include bifidobacteria, bacteroides, clostridia and streptococci. After weaning, a pattern resembling adult flora becomes established.

The gastrointestinal (GI) microflora play a major role in salvaging energy through the fermentation of dietary residues (mainly carbohydrates) that escape digestion in the upper GI tract. The main end products of fermentation in the colon are short-chain fatty acids (SCFA), such as acetic, propionic and butyric acids. The process of fermentation induces a number of changes in the metabolic environment of the gut lumen that are believed to be beneficial to health. These include a lowering of the pH (increased acidity), increase in faecal water, a decrease in its toxicity and, sometimes, laxative properties, including softening of faeces. A stimulation of colonic mineral absorption (magnesium, calcium) also has been described.

The different components of the colonic microflora exist in a delicate balance. Some bacteria are considered beneficial (e.g. bifidobacteria and lactobacilli), and others benign (e.g. certain eubacterium). Both types of bacteria are believed to suppress the growth of a third group of bacteria that are harmful to human health. These harmful bacteria include the proteolytic bacteroides species, *Clostridium difficile*, *Clostridium perfringens*, sulphate-reducing bacteria and the pathogenic species of the enterobacteriaceae. Thus a symbiosis has evolved between the host and its gut microflora. Increasing evidence suggests that GI well-being and function may be compromised by modern lifestyles (e.g. eating habits, antibiotic use, or stress) and that this is related to disturbances in gut microflora composition and function.

The gut microflora provide the basis for the gut barrier that prevents harmful bacteria from invading the GI tract. Moreover, it plays a major role in implementing, at an early age, an immune system in which resistance to infection and tolerance to antigens are balanced. The intestinal microflora, together with the gut's own immune system, allow the resident bacteria to perform a protective function.

### **Functional foods to promote gut health**

Three dietary strategies promote a healthier balance of gut microflora, namely, probiotics, prebiotics and synbiotics, and all have great potential as functional food components. Implicit in the definitions of all three is an alteration of the human gut microflora toward a more beneficial composition, usually effected by increases in bifidobacteria and/or lactobacilli.

In both human and veterinary health care, supplements containing bacteria with proven health supporting properties are sometimes administered in an effort to

replace or augment the normal gut species. Such supplements are called probiotics. By definition, a probiotic is a live microbial food ingredient that, when ingested in sufficient quantities, exerts health benefits on the consumer. Probiotics may have benefits both for healthy people and for those with medical problems, by acting either directly or indirectly via interactions with the gut microflora.

A prebiotic is a nondigestible food ingredient that beneficially affects the host by selectively stimulating growth and/or modifying the metabolic activity of one or a limited number of bacterial species in the colon that have the potential to improve host health. A synbiotic is a mixture of probiotics plus prebiotics and is directed at the increased survival of health-promoting bacteria, with an ultimate goal of modifying the gut flora and its metabolism (see page 24 for additional details of probiotics and prebiotics).

### ***Cognitive and mental performance***

Some foods or food components are not directly related to disease or health in the traditional sense but, nevertheless, provide an important function in changing mood or mental state. Behaviour is probably the most varied and complex of all human responses. This is because it is the cumulative outcome of two distinct influences: biological factors (including genetics, gender, age, body mass, etc.) and sociocultural aspects (including tradition, education, religion, economic status, etc.).

Effects on behaviour, emotional state, and cognitive performance call for food components that create both a short-term sense of feeling well and a long-term sense of being well or healthy. Because of this, perceptions about the effects of such food components are characterised by a high degree of subjectivity, with large differences in response among people. Age, weight and sex are

## 14 Concise Monograph Series

probably among a number of crucial parameters to take into account when evaluating the power of food components to alter behaviour.

Several aspects of behaviour are affected by foods. These include sensations, perceptions, moods and many mental functions, such as vigilance, memory, attention and reaction time. As mentioned previously, it is important to discriminate between two types of effects: the immediate effects, such as those on reaction time, attention focus, appetite and satiety, and longer-term effects, such as changes in memory and mental processes in ageing. The effects seen immediately after the first time that certain food components are ingested may be different from the longer-term effects of the same food component as a part of the habitual diet. Adaptation effects are a crucial aspect of all agents that are likely to modify appetite (palatability enhancers, artificial flavours, colours, etc.) and satiety (e.g. fibre content). It is these long-term chronic effects that will also determine whether certain food components can make successful functional foods. If palatability enhancers (e.g. fat substitutes) make it easier to eat more, or if intense sweeteners lead to an increased proportion of fat in the diet, then consumers may prefer not to have these in their regular diets, despite their immediate appeal.

### **Functional foods to promote optimal mental performance**

Some functional foods – such as the magic lunch food that will not induce or might even prevent a dip in vigilance in the post-lunch period – are desirable to everyone. Other foods will be functional for students who want to face exams with the maximum intellectual readiness; for those people with depression who expect relief from ingesting certain substances such as chocolate, sugars or

alcohol; or for the elderly and others who have failing memory. In the field of behaviour and mental functions, identifying the target consumer is very important.

Through an elevation in blood glucose, carbohydrates exert general beneficial influences on various aspects of mental performance, including improvements in working memory and decision time, faster information processing and better word recall. Caffeine also can lead to an improvement in most measures of cognitive performance (reaction time, vigilance, memory and psychomotor performance), especially in the morning hours.

High-carbohydrate meals help to produce feelings of drowsiness, sleepiness and calmness. In addition, the amino acid tryptophan reduces sleep latency and promotes feelings of drowsiness and fatigue in both adults and children. Tyrosine and tryptophan may help in recovery from jet lag, but only a small amount of scientific evidence supports this effect.

Sweet foods, such as sucrose, may relieve distress in young infants, and activation of endogenous opioids (beta endorphins) may reduce pain perception in members of the general population.

Intake of alcohol is both traditional and widespread in Europe. It is one of the few substances to affect all major areas of psychological and behavioural functions (appetite, cognitive performance, mood and stress), and the effects are conspicuously dependent on the dose.

A number of specific food components, such as choline, caffeine and some amino acids, are currently being studied to evaluate their effects on mood and cognitive performance. The outcomes of these studies will determine their possible use in functional foods.

## ***Physical performance and fitness***

During physical stress such as exercise, demands are high for food components (the substrates) that act as the starting material for reactions that release energy. A balanced diet with a carefully planned mix of food components can play a crucial role in improving the level of performance.

Training and competition will increase the daily energy expenditure by between 500 and 1000 kcalories per hour of exercise, depending on intensity. Large sweat losses may pose a risk to health by inducing severe dehydration, impaired blood circulation and heat transfer. This may ultimately lead to heat exhaustion and collapse. Insufficient replacement of carbohydrates may lead to low blood glucose levels, fatigue and exhaustion.

An ever-increasing amount of daily, high-intensity training leads to high stress on the metabolic machinery – the musculoskeletal and hormonal systems. A growing body of evidence supports observations that the supply of food ingredients or food-derived substances may interact with the biochemical and physiological systems involved with physical and mental performance. The results may impair recovery from intensive training and, hence, affect the physical well-being and health of the athlete.

### **Functional foods to promote optimal physical performance and recovery**

Requirements for specific nutrients and water depend on the type, intensity and duration of physical effort. Specific nutritional measures and dietary interventions can be devised to be appropriate for the distinct phases of preparation, competition and recuperation.

Oral rehydration products for athletes were one of the first categories of functional foods and drinks for which

scientific evidence was obtained on all levels of functionality. Among these functions are rapid gastric emptying, fast intestinal absorption, improved water retention, improved thermal regulation, improved physical performance and delayed fatigue.

Intense endurance exercise causes changes in the function of the GI system. Liquid food formulae, established to deliver fluid, glucose and electrolytes in a convenient and easily digestible form, have been shown to be of benefit to athletes. Exercise-induced losses of nitrogen, minerals, vitamins and trace elements should be replenished by ingesting larger amounts of high-quality, micronutrient-dense foods at meal times. However, this may be difficult in those circumstances in which low-energy diets are combined with intense training or in the case of multiple-day events, such as cycling competitions.

The use of special meals or food products and micronutrient supplementation will help ensure adequate intakes under these conditions. Specific types of carbohydrates with moderate-to-high glycaemic index in combination with protein have been shown to enhance recovery of athletes, and this offers potential for the development of functional foods.

## **HOW DOES THE CONSUMER LEARN ABOUT THE HEALTH BENEFITS OF FUNCTIONAL FOODS?**

---

### ***What are claims?***

The previous sections have outlined some of the important links between functional food components and health or performance. But how can consumers learn of these benefits? Health-related claims on food products and in advertisements and accompanying literature can play an essential role in communication. In fact, some people believe that functional foods should be defined as those foods that are accompanied by a health claim or a performance-benefit statement. It is, however, better to use the definition of functional foods as given in Section 1 and think of claims as a form of communication about functional foods.

The fundamental principle that any claim must be true and not misleading must apply to claims about health benefits. All such claims, therefore, should be scientifically valid and clear to the consumer. The key issue, however, is how this basic principle should be safeguarded without becoming a disincentive for the development and production of functional foods (an important determinant in trying to achieve the goal of improved public health) or for the acceptance of these foods by consumers (the ultimate target for the functional benefit).

This section will present claims that might be made for functional foods intended for the general population. This discussion will not include the so-called dietetic foods, which are foodstuffs intended to satisfy the

nutritional requirements of specific groups of the population and are subject to specific EU directives (see Box 2). Dietetic foods (originally known as PARNUTS foods) are intended for individuals with a specific disease or condition, whereas functional foods are intended for basically healthy consumers who want to remain healthy. Marketing of dietetic foods is mainly directed to health professionals, whereas marketing of functional foods is directed at the consumer.

### **BOX 2**

#### ***Distinction between functional and dietetic foods***

The terms “functional foods” and “dietetic foods” are sometimes confused. However, the latter are legally defined, whereas the former have no legal standing, as yet. The so-called dietetic foods are intended to satisfy particular nutritional requirements of specific groups of the population. Examples of dietetic foods are:

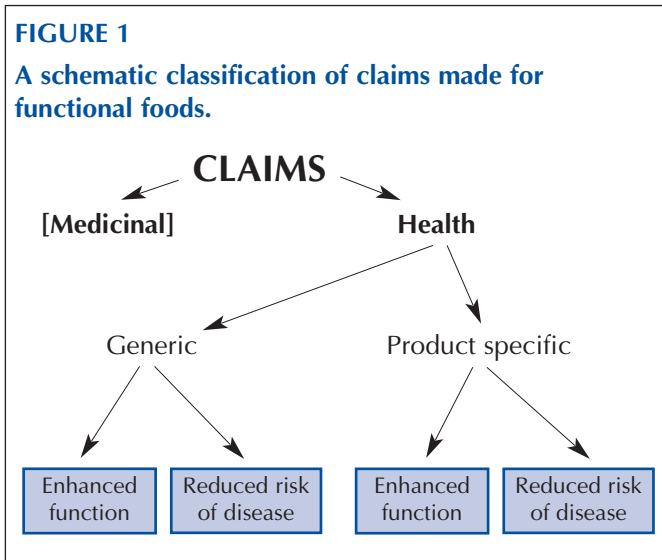
- Foods for infants and young children, including infant formulae and follow-on formulae, processed cereal-based foods and baby foods (weaning foods).
- Foods intended for use in energy-restricted diets for weight reduction.
- Foods for sports people.
- Foods for special medical purposes.

An over-arching European Union (EU) directive (EU Framework Directive 89/398/EEC and its amendments 96/84/EC and 1999/41/EC) sets out the definition of dietetic foods and certain labelling requirements. A set of specific directives outlines rules for the composition, marketing and labelling requirements of certain dietetic foods, including measures to ensure the appropriate use of such foods and to exclude any risk to human health.

The nutritional substances that can be added to dietetic foods are controlled either through positive lists included in the specific directives or by a special Commission Directive. These apply to all other dietary food groups covered by specific directives. The directives are based on scientific advice from the Commission's expert committees.

## Types of claims

It is important to distinguish different types of claims. Figure 1 shows a simple classification of functional claims.



The first distinction is between health claims and medicinal claims. The latter are currently prohibited world-wide for food products, including drinks and food supplements.

A medicinal claim states or implies that a food has the property of treating, preventing or curing human disease or makes a reference to such a property. Human disease means any injury, ailment or adverse condition, whether of body or mind. All food products are prohibited by food law from making direct or implied medicinal claims (i.e. claims for the prevention, treatment or cure of disease). However, in the absence of an EU-wide definition of “prevention” or “disease”, member states have been free to interpret this prohibition in their own way, sometimes very broadly. Depending on country regulation, the use of some specific words, such as restore, repair, eliminate,

control, normalise or strengthen, is not allowed if these words signify that a product can treat, prevent or cure human disease or imply that the product can provide a medicinal benefit.

In a few cases, medicinal licences have been granted for certain food supplements. An example of a medicinal claim that can be used by such a company is: “Folic acid may prevent neural tube defects”.

A health claim is a direct, indirect or implied claim in food labelling, advertising and promotion indicating that consumption of a food carries a specific health benefit or reduces the risk of a specific health detriment.

### *What is the difference between generic and product-specific (innovative) health claims?*

**Generic health claims** are based on a consensus in the scientific community about a well-established, generally accepted diet–disease or diet–health relationship. Such claims can be used for any product, provided that it fulfills certain compositional criteria. Generic claims are based on knowledge from evidence in the scientific literature and/or on recommendations from national or international public health bodies, such as the United States Food and Drug Administration (FDA), the EU Scientific Committee for Food (SCF) or the United Kingdom’s Scientific Advisory Committee on Nutrition (SACN). Examples include claims such as: “Soy protein can help reduce LDL cholesterol”, and “Dietary fibre can help maintain a healthy gut”.

**Product specific (or innovative) claims** imply that the food product has certain physiological effects. The claims require demonstration of such effects when the specific food product is consumed in realistic amounts. Examples include claims such as: “Product X can help

reduce LDL cholesterol”, and “Product Y can help maintain a healthy gut”.

Both generic and innovative health claims can be subdivided into two types, enhanced function and reduction of disease risk, according to the specific effects that are claimed.

### ***What is the difference between “enhanced function” and “reduction of disease risk” claims?***

**Enhanced function** claims concern specific beneficial effects of foods, nutrients, components or ingredients on physiological or psychological functions or biological activities beyond their established role in growth, development and other normal functions of the body. These claims relate to an improvement in healthy conditions and contain no explicit references to the risk of a specific disease. Examples of such claims include: “Certain nondigestible oligosaccharides may improve the growth of a specific bacterial flora in the gut”, “Caffeine can improve cognitive performance”. and “Folate can help maintain healthy plasma homocysteine levels”.

**Reduction of disease risk** claims relate to the consumption of a food, nutrient, component or ingredient that may help reduce the risk of a specific disease or condition. Such a claim is genuinely different from the medicinal claim to prevent a disease. The most important difference is that the concept of reduction of disease risk takes into account the complexity and multifactorial basis of most diseases as well as the complexity of the diet itself.

The concept of reduction of risk of a disease may lead to the development of functional foods that, if consumed on a regular basis as part of the diet, will help reduce significantly the risk of a disease for which a relationship with dietary intakes has been documented. For instance, such foods might do this by improving / rebalancing metabolic processes or strengthening natural defence mechanisms. A nutrition-based approach is aimed at a broad group of people to produce future, long-term benefits.

These claims correspond most closely to those referred to as “health claims” in the United States. Examples of such claims include: “Folate may reduce a woman’s risk of having a child with neural tube defects”, “Sufficient calcium intake may help to reduce the risk of osteoporosis in later life”, and “Intake of specific probiotics may help to reduce the risk of rotavirus infection in young children”.

### **Developments within the CODEX Alimentarius**

The Codex Alimentarius has proposed several versions of draft guidelines that apply to health claims and has identified three types of claims: nutrient function claims, other function claims and reduction of disease risk claims (Table 2). The 2002 Codex proposals are generally similar to the enhanced function claims and reduced risk of disease claims suggested in the FUFOSSE Consensus Document, although some of the details and terms differ. In fact, the Codex “other” function claim was called enhanced function in previous draft guidelines.

**TABLE 2****CODEX Alimentarius: Proposed draft guidelines for the use of health and nutrition claims (2002)**

TYPE OF CLAIM	DEFINITION	EXAMPLES
<b>Nutrition claim</b>	<i>Any representation that states, suggests or implies that a food has specific nutritional properties including but not limited to the energy value and content of protein, fat and carbohydrates, as well as the content of vitamins and minerals.</i>	
Nutrient content claim	A nutrition claim that refers to the level of a nutrient contained in a food.	“Source of calcium”, “high in fibre”, “low in fat”
Comparative claim	A nutrition claim that compares the nutrient levels and/or energy value of two or more foods.	“Reduced”, “less than”, “fewer”, “increased”, “more than”
<b>Health claim</b>	<i>Any representation that states, suggests or implies that a relationship exists between a food or constituent of that food and health.</i>	
Nutrient function claim	A form of claim that refers to the physiological role of the nutrient in growth, development and normal functions of the body.	“Food X is a good/excellent source of nutrient A, (naming the physiological role of nutrient A in the body in the maintenance of health and promotion of normal growth and development)”.
Other or enhanced* function claim	Claims that concern specific benefits of the consumption of foods and their constituents in the context of the total diet for physiological or psychological functions or biological activities but that do not include nutrient function claims. Such claims relate to a positive contribution to health, improvement of a function, or modification or preservation of health.	“Food Y contains x grams of substance A, (naming the effect of substance A on improving or modifying a physiological function or biological activity associated with health)”.
Reduction of disease risk claim	Claims relating the consumption of a food or food constituent in the context of the total diet to the reduced risk of developing a disease or health-related condition. The claim must consist of two parts: (1) information on an accepted diet-health relationship, followed by (2) information on the composition of the product relevant to the relationship, unless the relationship is based on a whole food or foods whereby the research does not link to specific constituents of the food.  Risk reduction means significantly altering one or several risk factors for a disease or health-related condition. Diseases have multiple risk factors, and altering one of these risk factors may or may not have beneficial effects. The presentation of risk reduction claims, e.g., must ensure, by use of appropriate language and reference to other risk factors, that consumers do not interpret them as prevention claims.	“A diet low in substance A may reduce the risk of disease D. Food X is low in substance A”. “A healthful diet rich in substance A may reduce the risk of disease D. Food X is high in substance A”.

(\* previous drafts have used this term)

## HOW SHOULD CLAIMS BE SUBSTANTIATED AND APPROVED?

### Substantiation of claims

If consumers are to benefit from truthful health claims, there must be guidelines to follow for those wishing to make a claim. Several countries have now developed codes of practice. The Council of Europe has also developed guidelines concerning the scientific substantiation of health-related claims for functional foods. The following is a simplified version of these guidelines to indicate the type of submissions that might be required by all authorities. Three main issues to consider are outlined in Table 3 and discussed in the following text.

#### Totality of the evidence

Substantiation of a health claim should be based on a systematic review of the evidence relevant to the claim. The scientific evidence to substantiate a health claim is

### TABLE 3

#### Checklist for the substantiation of claims

- What is the totality of the evidence? Is the submitted evidence obtained from human studies that are methodologically sound and most relevant to the claim?
- What is the validity of the evidence?
- Have the right conclusions been drawn from the evidence?

likely to be drawn from three general types of studies. These are shown in Table 4, ranked according to the preferred hierarchy of their value in substantiating a health claim.

A health claim should be based on those studies in humans that are the most methodologically sound. In general, experimental or “intervention” studies in humans are more useful than observational studies when substantiating a claim. This is because experimental studies are less susceptible to bias (i.e. the researcher can be more certain that any measured effect, e.g. on a marker for a target function, is attributable to the specific intervention, such as a functional component, and not to other factors). But some designs for experimental studies are more susceptible to bias

### TABLE 4

#### Hierarchy of evidence from different types of studies to support claims (beginning with the most preferred)

Experimental human trials (sometimes referred to as clinical or intervention studies)

- Randomised controlled intervention studies
- Less well-controlled types of intervention studies

Observational human studies (sometimes referred to as epidemiological studies)

- Prospective cohort studies
- Retrospective cohort studies
- Case-control studies (always retrospective).

Biochemical, cellular or animal studies

than others. In good experimental studies, subjects are purposely allocated to different groups (normally an “intervention” group or groups and a “control” group) and exposed to different conditions (such as different diets or diets containing different functional components). The most reliable method of assigning subjects to different groups is by random allocation. This allocation ideally should be concealed from both investigators and subjects (the double blind method). The double-blind, randomised intervention study (otherwise known as the double-blind, randomised controlled trial or RCT) is a very efficient way to get evidence for the effects of a functional food component on a target function.

Similarly, some designs for an observational study are more reliable than others. Studies planned in advance and undertaken prospectively (cohort studies) are less likely to be biased than studies that are carried out retrospectively (case control studies). Cohort studies are those in which groups of individuals who vary their exposure to different conditions are followed to assess what happens to them. Case control studies are those in which individuals who have experienced a specific effect or suffer from a specific disease are compared with individuals without similar experiences or diseases. In general, claims should be substantiated using studies from the top of the hierarchy. However, care should be taken in using this hierarchy of evidence, because validity depends not only on the type of study but also on how well it was designed, carried out and analysed. A badly executed double-blind RCT may be less valid than a well-conducted case control study.

### **General principles for ensuring the validity of studies**

For studies used to substantiate health claims (whether these are experimental or observational), validity is improved if:

- The subjects are representative of the target group for the claim.
- The subjects consume a reasonable amount of the food or food component in question at a reasonable frequency, consistent with realistic consumption patterns.
- The study is large enough to demonstrate the proposed beneficial effect. The desirable size for a study can be assessed using standard formulae for power analysis.
- The duration of the study is long enough to justify any implication of the claim that a beneficial effect is a long-term rather than a short-term effect.
- The outcomes are measured properly and according to standard procedures.
- The outcomes are identical or similar to those of the claimed effect. If the claim refers, e.g., to a risk factor for a disease, then at least some of the studies used to substantiate the claim should involve measuring that risk factor.
- Possible confounding variables are taken into account. In a study of the association between a food or food component and a beneficial effect, confounding can occur when the studied population is simultaneously exposed to something else (e.g. an unavoidable change in total fat intake when looking for an effect of increasing the n-3 PUFA content of the diet) that could be associated with the proposed cause and effect.

**Validation based on markers of enhanced function or reduced disease risk: the FUFOSE proposal**

*Types of markers*

In most cases, the scientific substantiation of a health claim is a difficult and time-consuming exercise. It requires a solid scientific basis to show that, without doubt, certain food components and other food properties can enhance function or reduce the risk of disease. The whole process, however, can be speeded up and simplified by identifying 'markers' that relate to exposure, enhanced function and reduced risk of disease (Table 5). In general, the identification and validation of these markers is based on research from many centres and is subject to a scientific consensus.

<b>TABLE 5</b>
<p><b>Types of markers</b></p> <p><b>Markers of exposure</b>, such as those evaluating digestibility, fermentability, absorption and/or tissue distribution or, in general terms, biological accessibility.</p> <p><b>Markers of target functions and biological responses</b>, such as changes in body fluids or tissues, levels of a metabolite, a protein or an enzyme, or markers that relate to a change in a given function such as muscular strength, maximal oxygen consumption, cognition or gut transit.</p> <p><b>Markers of intermediate endpoints of an improved state of health and well-being and/or reduction of a disease risk</b>, such as the measurement of a biological process that relates directly to the endpoint (e.g. measurement of haemoglobin levels for anaemia or measurement of vessel wall thickness for cardiovascular disease).</p>

Markers can be biochemical (e.g. a change in an enzyme) or physiological (e.g. the change in the function of a body organ) in nature. They may be based on an objective assessment of body functions, such as psychological and physical performance or a subjective assessment of quality of life. The marker(s) based on dynamic response are often as useful as or even more useful than static measurements, e.g., the measurement of blood lipids after a meal (dynamic marker) rather than fasting levels (static marker). In many cases, a consistent response of a convergent battery of markers may provide more definitive evidence of functional and health benefits, because it evaluates different aspects of the same function and, thus, better targets the function and its modulation.

*Linking evidence based on markers to possible claims*

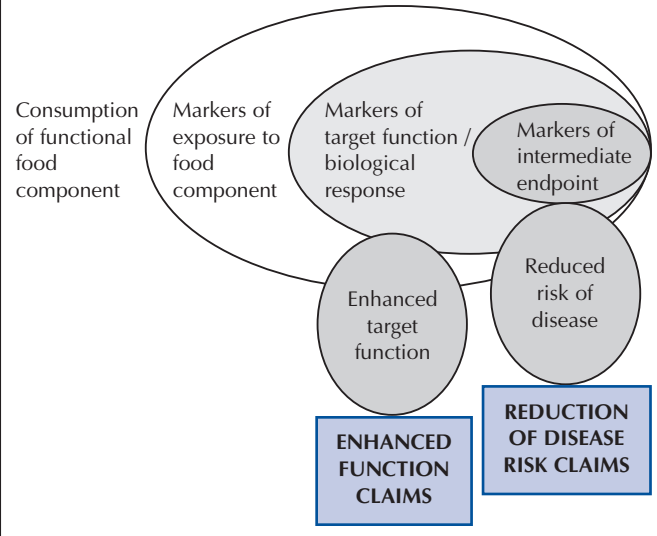
The innovative proposal from the ILSI Europe – coordinated Concerted Action on Functional Food Science in Europe, put forward in the FUFOSE Consensus Document, was that specific validated markers can be used for substantiation of health-related claims for specific foods by using them in properly designed human studies (Figure 2).

Claims should be based on evidence related to markers that are linked to clearly defined and measurable outcomes and are significantly and consistently modulated by the particular food component in rigorously controlled studies. If evidence is based on a marker of enhanced function, then an enhanced function claim can be made. If evidence is based on a marker of reduced risk of disease, then only in this case can a reduction of disease risk claim be made.

It is important to recognise that the FUFOSE scheme would produce claims that, in some cases, differ from those in the United States, even if the submission is based

FIGURE 2

**Functional foods: a proposal for a scientific basis for claims (from FUFOSE Consensus Document).**



on similar scientific evidence (see Box 4). If evidence suggests, e.g., that a product can lower blood levels of cholesterol, an enhanced function claim along the lines of “maintains healthy levels of cholesterol” is suggested. In contrast, in the United States, a generic claim for reduced risk of heart disease can be related to components that lower the blood cholesterol level, such as saturates, oat and psyllium fibre, soy protein and plant sterols/stanols. This is the most important aspect of the FUFOSE scheme, relating the type of claim made to the type of marker upon which the evidence is based.

### ***Drawing conclusions from the evidence***

Conclusions drawn from the totality of evidence and from studies that are the most methodologically sound will be more valid if the results are in line with the marker criteria described in Table 6.

## ***Systems for approval of health claims***

Whatever the regulatory system (*a priori*, *a posteriori*, voluntary code of practice, or imposed by law), the totality of evidence should be evaluated according to the usual standards of scientific peer review. The peer review of data available to substantiate a health-related claim should be performed by an independent group of appropriately qualified experts who deliver a recommendation on whether the claim meets the scientific criteria to be regarded as acceptable. The procedure should be transparent and provide the initiators (those submitting the claim) with all the elements of the reasoning behind the verdict.

TABLE 6

### **Criteria for good markers**

- Markers should be feasible (i.e. measurable in easily accessible material or obtainable using ethical or minimally invasive methodology), valid, reproducible, sensitive and specific, plausibly linked to the phenomena involved in the biological process being studied and should represent relatively immediate outcomes that can be used to assess interventions in a reasonable timescale.
- Markers should be rigorously internally validated to establish sensitivity (the frequency of a positive test result when the effect is present), specificity (the frequency of a negative test result when the effect is absent) and reproducibility in different centres.
- Markers should be generally accepted in the scientific field as valid in relation to the function and/or disease risk.
- The effect measured by the selected marker should be physiologically and statistically significant.

## ***SOME EXAMPLES OF FUNCTIONAL FOOD COMPONENTS***

---

Section 3 of this concise monograph discussed the general principles behind health claims and how such claims should be substantiated according to the scientific evidence. In this section, two examples of functional food components will be discussed in detail. These examples have been chosen because they relate to entirely different areas of physiology and illustrate the wide potential for development of functional food components. They are: (1) the ability of plant sterol and stanol esters to reduce LDL cholesterol; and (2) the ability of probiotics and prebiotics to promote a beneficial balance of gut microflora.

### ***Plant sterol and stanol esters***

#### **Background**

It has been known for 50 years that plant sterols, which play a similar role in plants to that of cholesterol in animals as a metabolic precursor and structural molecule, can interact with cholesterol in the intestinal tract to effect a reduction of cholesterol absorption and a subsequent reduction in blood cholesterol. However, for technical reasons, this finding has been exploited only recently. The esterification of plant sterols allows them to be solubilised in the matrix of food fat and so incorporated simply and effectively into the diet. The sterols themselves may be esterified in their natural state or after hydrogenation (plant stanols).

Plant sterols are natural constituents of plants, including trees and a number of common crops, such as soya and maize, and these provide the sources for food use.

However, they are generally present in the diet at relatively low concentrations. Ordinary diets may provide around 200-400 mg/day, although vegetarian diets may contain up to 800 mg/day.

#### **Substantiation of claims for plant sterols and stanols**

A number of studies have demonstrated the ability of plant sterols/stanols to reduce LDL cholesterol under various conditions. Studies have been conducted in men and women with normal and high levels of blood cholesterol, in adults consuming low- and high-fat diets, in people taking drugs to lower cholesterol and in children with inherited levels of high cholesterol. The results are generally consistent, showing that plant sterol/stanols reduce LDL cholesterol by around 10%–15%, with a dose-response effect. Daily intakes above 1.6 g are needed for an effect, and a plateau is reached at levels of about 2 g/day. No effect on HDL cholesterol has been found, and sterols

### ***BOX 3***

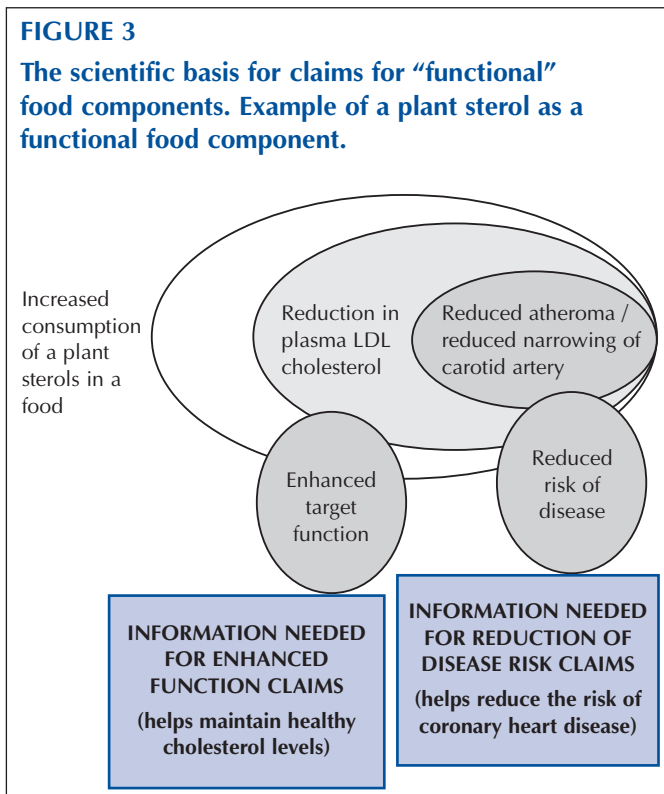
#### ***Functional foods and diet-gene interactions***

Several examples illustrate the way in which the genetic make-up of the individual can determine disease risk and influence the effect that dietary components have on biological markers for function and disease. These are not rare cases. Indeed, in one such example of a genotype determining blood cholesterol, people with genotype X (>25% of the population) have been shown to be more at risk of heart disease than are people with genotype Y. Some evidence suggests that this genotype also determines the degree to which an individual's blood cholesterol level is lowered by a reduction in dietary saturates and also by plant sterols. Consequently, those people with genotype X will probably benefit most by taking plant sterols within a diet that is low in saturates.

Additional evidence along these lines will help to show there is no conflict between those who promote a general healthy diet and those who promote functional foods. The two activities are very much complementary.

and stanols appear equally effective. The beneficial effect of plant sterols also appears to be influenced by the genotype of the individual (Box 3),

Section 3 of this monograph introduced the FUFOSSE proposal (Figure 2) for the validation of claims based on appropriate markers. Figure 3 shows how this scheme could be applied to collect the scientific evidence to make claims about a product containing plant sterols. If sufficient evidence suggests that a product containing a plant sterol or stanol ester could lower LDL cholesterol, this could be used to support an enhanced function claim, such as “maintains healthy cholesterol levels”. This evidence alone could not be used to make a reduced risk of disease claim, because however good the relationship



## BOX 4

### Europe and the United States

The health claim suggested by the FUFOSSE proposal would differ from the FDA-approved claim for plant sterol and stanol esters in the United States. The FUFOSSE scheme suggests only an enhanced function claim, because the evidence for the efficacy for sterols and stanols is based on lowering LDL cholesterol levels and because the FUFOSSE scheme is clear that the claim should be based on the marker. As yet, no direct evidence of reducing CHD incidence or morbidity has been produced. The FDA scheme does not require this link to specific markers. Permissible statements in the United States are along the following lines “Foods containing at least 0.65 grams per serving of plant sterol esters, eaten twice a day with meals for a daily total intake of at least 1.3 grams, as part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease”.

Another key difference between the FUFOSSE proposal (and some other European developments) and the FDA system is that the European schemes require scientific substantiation of food products as the basis for product-specific claims, whereas the FDA system currently allows generic claims based on the content of the active substance and some general requirements on the nutritional composition of the product.

between LDL cholesterol and CHD might be, it is only one of the many risk factors for CHD (see Box 4). To make a claim that the product could “reduce the risk of CHD”, adequate evidence would have to substantiate the assertion that the product, e.g., could reduce the wall thickness of the carotid artery. This marker, reflecting atheroma in the carotid and presumably other arteries, would probably be acceptable as a marker of reduced risk of CHD.

### Safety

The safety of plant sterols has been assessed in the United States, where products containing them have “generally recognised as safe” (GRAS) status, and in the EC by the SCF. There appear to be no toxicity issues associated with

their consumption, although a significant reduction of circulating beta carotene concentrations (but not those of other carotenoids that are less lipophilic) has been observed. The reduction, however, is biologically modest and less than the typical seasonal variation. Concentrations can be restored by consuming the recommended levels of fruit and vegetables. Additional safety monitoring will be needed, especially if high levels of consumption occur as these ingredients appear in more and more products.

### **Practical aspects**

The fat spreads now available have enhanced levels of plant sterols and stanols (8 g/100g), so that a typical daily serving of 20-25 g provides the equivalent of 1.6-2.0 g plant sterol/stanol.

## ***Probiotics and prebiotics as functional food components***

### **Background**

#### ***The concept of balanced gut microflora***

To understand the basis for the development of prebiotics and probiotics as functional food components, a brief familiarity with the gut and its microflora is needed.

The gut is an obvious target for the development of functional foods, because it acts as an interface between the diet and all other body functions. The development of gut microflora provides the basis for the gut barrier that prevents pathogenic bacteria from invading the GI tract and eventually the circulating blood and the entire body. The balance of intestinal microflora, together with the gut's own immune system, allows the resident bacteria to have a protective function, especially against the proliferation of pathogens.

Apart from its barrier function against infection, the intestinal microflora salvages energy through fermentation of carbohydrates that are not digested in the upper gut. This also produces SCFAs, which play various important metabolic roles. The main substrates for bacterial fermentation are endogenous carbohydrates (e.g. mucus) and dietary carbohydrates that have escaped digestion. These include starch that enters the colon (resistant starch), as well as nonstarch polysaccharides (e.g. celluloses, hemicelluloses, pectins and gums), non-digestible oligosaccharides and hydrogenated carbohydrates (such as polyols). In addition, proteins and amino acids can be used as growth substrates for colonic bacteria. Total substrate availability in the human adult colon is 20-60 g carbohydrate and 5-20 g protein per day. Both large bowel integrity and colonic microflora are important in determining stool characteristics, such as weight, consistency, frequency and total intestinal transit time – perhaps the most reliable markers of general colonic function.

A third important function of the beneficial gut microflora is its ability to metabolise and detoxify potentially harmful compounds such as carcinogens.

#### ***Gut microflora composition***

Bacterial numbers and composition vary considerably along the human GI tract, but the large intestine is by far the most intensively populated microbial ecosystem, with several hundred species accounting for a total of between  $10^{11}$  and  $10^{12}$  bacteria per gram of contents. Quantitatively, the most important genera of intestinal bacteria in humans are the bacteroides and the bifidobacteria, which can account for 35% and 25%, respectively, of the known species. The microflora of the large intestine is acquired at and shortly after birth, and is modulated by the host and the diet. After weaning, a new adult-like equilibrium is set up, depending again on the host and diet. This means that each individual has his or her own specific gut microflora, which, in individuality, is comparable to a fingerprint.

The gut microflora is a complex interactive community of organisms, and its functions are a consequence of the combined activities of all the microbial components. The group of potentially health-promoting bacteria are believed to include principally the bifidobacteria and lactobacilli. It is commonly agreed that gut microflora can play an important role in GI infections, constipation, irritable bowel syndrome, inflammatory bowel diseases and, perhaps, colorectal cancer.

The composition and the metabolic and enzymatic activity of the faecal microflora, when analysed correctly, are good markers of the status of the resident gut microflora. Traditional gut microbiological methodologies are based on morphological and biochemical properties of the organisms. However, recent advances in molecular genetics for quantitative and qualitative monitoring of the nucleic acids from human gut microflora have revolutionised their characterisation and identification.

### Substantiation of claims for probiotics and prebiotics

One of the most promising areas for the development of functional food components lies in the use of probiotics and prebiotics to modify the composition and the metabolic and enzymatic activities of the gut microflora.

Probiotics have been defined largely on the basis of their various original uses in animal feeds. None of these definitions is satisfactory for the purpose of human nutrition. It is now suggested that a probiotic is best defined as “a live microbial food ingredient that, when ingested in sufficient quantities, exerts health benefits on the consumer.”

Various species of lactobacilli and bifidobacteria combined (or not) with *Streptococcus thermophilus* are the main bacteria used as probiotics in yoghurts or fermented dairy products. Their major health benefits,

demonstrated in humans, are alleviation of lactose intolerance and immune stimulation to reduce the incidence or severity of GI infections. They also have been shown to reduce the incidence of precancerous lesions in carcinogen-treated animals, but research in clinical trials still must confirm the importance of this observation for humans. Because the probiotic bacteria are only transient in the intestinal tract and do not become part of the host's gut microflora, regular consumption is necessary for the maintenance of favourable effects.

An additional mechanism by which probiotic bacteria may promote health in the digestive tract is by altering the local immune response. Survival of the bacteria during intestinal transit and adhesion to intestinal cells seem to be important for modifying the host's immune reactivity. A favourable modification of immune responses after the ingestion of probiotics or their extracts has been reported in animal and human studies.

A prebiotic is a “nondigestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or modifying the metabolic activity of one or a limited number of bacterial species in the colon that have the potential to improve host health”. Key criteria for a food ingredient to be classified as a prebiotic is that it must result in a significant transfer to the colon and must not be hydrolysed or absorbed in the upper part of the GI tract. It must be a selective substrate for one or more beneficial bacteria that are stimulated to grow, and it may induce local (in the colon) or systemic effects through bacterial fermentation products that are beneficial to host health.

Apart from their potential to modify gut microflora and metabolic activities in a beneficial manner, many other helpful effects of prebiotics are being investigated. These include their ability to activate the immune system, increase the absorption of certain minerals such as calcium and inhibit lesions that are precursors of

adenomas and carcinomas. Thus, they could have the potential to help reduce some of the risk factors involved in the causes of colorectal diseases. Strategies for developing prebiotic products as functional foods should aim to provide specific fermentable substrates for beneficial bacteria such as bifidobacteria, lactobacilli and bacteroides. These may provide beneficial amounts and proportions of fermentation products, especially in the distal colon, where the effects are believed to be most favourable.

Figure 4 shows how the basic scheme relating claims to evidence based on relevant markers could be used to justify claims about a food product containing prebiotics. An enhanced function claim, such as “improves gut function”, might be made if sufficient evidence supported the assertion that consumption of the food could increase the faecal content of either lactobacilli, bifidobacteria or any other beneficial bacteria. This would probably be accepted as a marker of modified microflora. Even better, if the consumption of the food containing a prebiotic was shown to increase faecal mass and soften the stool, then this would certainly be accepted as a marker of enhanced function (i.e. improved gut function).

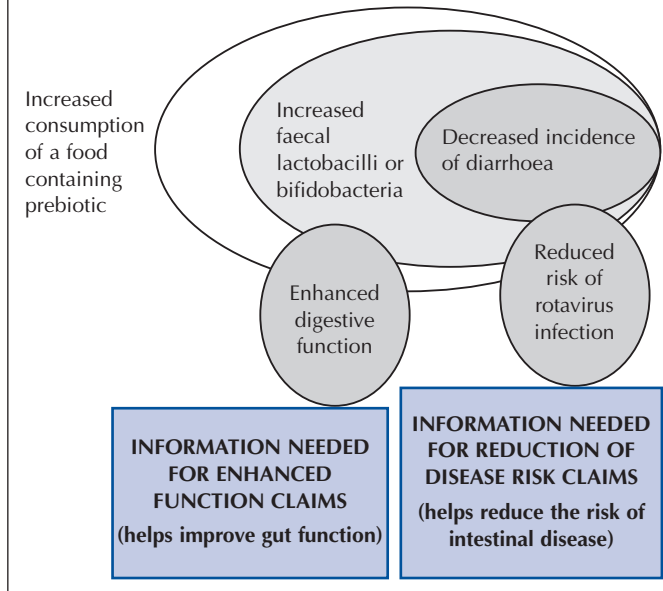
To make a claim that a product could reduce “the risk of intestinal disease”, adequate evidence would be needed based on the use of appropriate markers related to the selected disease risk factors.

## Safety

Many safety studies have been performed with probiotics, and these have been the subject of several recent reviews. A variety of strains of probiotic organisms have been used in the clinical treatment of GI disorders in both children and adults. These include conditions in which mucosal integrity is impaired. No evidence of opportunistic infections or other ill effects of probiotics have been observed in these studies.

**FIGURE 4**

**The scientific basis for claims for “functional” food components. Example of prebiotics.**



A large number of studies have also been performed on the effects of consumption of different types of prebiotics, both in animals and in humans. No single safety issue has been identified. Accordingly, they are universally used in many kinds of functional foods. The inulin-type prebiotics have been reviewed for safety by the ILSI North America Technical Committee on Food Components for Health Promotion in a Food Component Report.

## Practical aspects

The major applications for probiotics are in dairy foods. Prebiotic functional food components are found in dairy products, table spreads, baked goods and breads, salad dressings, meat products and some confectionery items.

## TECHNOLOGY IN THE DEVELOPMENT OF FUNCTIONAL FOODS

---

Food technology plays many major roles. The most important of these is to extend the period over which foods remain wholesome. In the past, methods to preserve foods protected people from the problems of nonavailability of food and the dominance that these problems had over their lives. In addition, it protected their health. Once conserved, greater varieties of foods can be stockpiled for times when food is scarce, meeting essential needs for safe sources of energy and providing for increased variety and healthfulness in the diet.

Over the last century, food technology has evolved to produce other essential attributes of preserved food, including palatability, convenience and the guarantee of nutritional quality. Today, with the growing emphasis on health and nutrition in functional foods, the traditional applications of food technology continue to evolve. Palatability and convenience remain the cornerstones of food products, but it is also clear that the interpretation of nutritional quality is becoming broader and requires proactive contributions from food technology.

The food industry is constantly updating food technologies for reasons of efficiency, safety and quality but it is innately conservative (for very good reasons, because safety must be uppermost). All food technologies are carefully evaluated before they enter into common use. Although the food industry uses technology to produce functional foods, it is very unusual for that technology to drive the development of a functional food.

Nutritional science has made great strides over the last century to identify nutrients and ingredients with specific

effects on health. These substances can be obtained from raw materials and incorporated into foods targeted to specific groups of consumers. Alternatively, if a naturally present component carries a negative effect on health, it can be eliminated. As regards the composition of functional foods, the long experience of food technology can be brought to bear on two main areas: fortification and extraction. Research and development activity for functional foods must be applied to their specific, and in some cases unique, composition (with emphasis on identification, acquisition, preservation and enhancement of functional properties), so that claims made to consumers to help communicate the benefits will be true.

### **Fortification**

Fortification and restoration are widely used terms in functional food technology. Fortification means enrichment of a product with a nutrient to a level that is higher than that normally occurring in the food in the unprocessed state. The term restoration is reserved for bringing back a nutrient or nutrients to the normal level, e.g. after nutrient loss during processing.

### **Nutrients used for fortification**

Vitamin and mineral fortification for specific purposes is already well known. Antioxidants are a good example of fortificants that have the potential to confer health benefits as constituents of functional foods. However, by their very nature, all antioxidants are capable of being oxidised. If this happens within the functional food, their biological antioxidant capability is likely to be lost. Oxidation is probably the most important cause of food degradation, and food technologists have spent many years understanding the phenomenon and developing strategies by which oxidation can be limited. These include oxygen- and light-resistant packaging, controlled atmosphere, gassing with inert nitrogen, encapsulation or

separation of sensitive ingredients and careful mixing and use of more labile antioxidants for protection. Today, these classic methods can be used to preserve the biologically important antioxidants in the same way they are used to preserve the food itself.

Folate (usually in the form of folic acid) has been added to foods in many countries in the last few years as a public health measure to reduce neural tube defects in newborn infants. Recent data from the United States have shown that this, indeed, has been successful in reducing the incidence of such defects. Folate also has been shown to play a role in reducing plasma levels of homocysteine, a risk factor for heart disease. More than 150 different forms of folate are known that can be more or less stable in foods. Folate can be lost from foods through heat treatment, contact with hot water (e.g. boiling or blanching) and contact with liquids that are not acidic. For this reason, dry foods, such as flour, cereals and bread, have been the main carriers for folate fortification. Nevertheless, ongoing research is assessing the effects of food processing on the stability and bioavailability of folates. Future developments in technology will certainly yield greater understanding of the relation between food processing and optimal folate delivery.

Fortification of food products with calcium is universally applied as one of the strategies to enhance calcium intake and improve bone mineral density. However, it is difficult to add calcium in significant quantities, because it often gives a chalky taste and a bad mouth-feel or because it precipitates into a greyish mass within a liquid product. However, judicious mixing and the use of different sources of calcium, interesting textures for the food itself, masking flavour substances and different combinations of ingredients can improve the palatability of calcium fortified foods. This clearly is a challenge for food technology.

### **Non-nutrients added to foods**

Phytochemicals are the major class of non-nutrients with potential use as functional food components (see Section 4), although some animal components from milk or fish also may have favourable health benefits when consumed in sufficient quantities.

As discussed in Section 4, bacteria and their byproducts are also of growing importance. Strains of beneficial living bacteria added to foods will compete in the gut with pathogenic bacteria, toxins and viruses and provide protection for the digestive tract. In addition, specific strains have been shown to have immune-stimulating effects. Ironically, food technology originated in finding ways to eliminate or control microbial contamination and guarantee safety of the food during its shelf life. Now, food technology is confronted with the challenge of finding ways to encourage survival of specific microbes while still keeping the pathogens under control. This is not a trivial exercise and requires some of the most creative approaches in food technology today.

### ***Extraction and separation***

Extraction and separation technologies can be applied to raw materials that are found to have special activity related to health and well-being. These functional components then can be added to food products (additions). Extraction and separation technologies also can be used for improvement of the food's contribution to health by eliminating a component that interferes with its optimal nutritional value (removals).

### **Examples of additions**

There are many possibilities using various typical extraction techniques from innumerable foods as starting material for additions. The soluble fibre "beta-glucan" can be extracted from grains and added to different foods to

give cardiovascular and gut health benefits. Isoflavones can be extracted from soy and added to products that target the reduction of osteoporosis, promotion of heart health and alleviation of menopausal symptoms for women. Glucosinolates from vegetables are being investigated as potential functional components on the strength of their enhanced hepatic and detoxification capacity. Milk has proved to be a tremendously rich source of ingredients such as lipids, including phospholipids, proteins and peptides, oligosaccharides and minerals. These ingredients can all be extracted and are used globally to increase the nutritional value of many different foods.

The plant sterol- and stanol-containing foods on the market in several countries around the world are examples of the first applications of extraction and addition technology in the functional foods arena. Sterols are obtained from a few plant sources using classic extraction techniques. They tend to have rather poor solubility in a lipid environment and are usually esterified with fatty acids obtained from vegetable oils to add them to products such as spreading fats. As discussed in Section 4 (see page 22), plant sterols may decrease cholesterol absorption by the gut, so that the blood cholesterol decreases.

### Examples of removals

Removal of ingredients that contribute to negative health effects is an older idea, but it nevertheless brings nutritional advantages. For some time, cholesterol extraction of egg yolks has been achieved by techniques such as supercritical carbon dioxide extraction to make eggs with improved health value.

Phytate is naturally found in cereals and acts as a chelator of trace elements, inhibiting their absorption and diminishing the nutritional value of cereals. Destroying

the phytate with phytase treatment improves the body's uptake of trace nutrients such as zinc and iron that are either added or intrinsic to the cereal.

### *Emerging technologies*

Functional foods are newly recognised for their potential to contribute to health, but the food processes that are used to manufacture them are essentially the same as those used for conventional foods. This said, food technology continues to advance in its efforts to develop better, faster, safer and more economical technologies. A good example is the technology of minimal processing, which has reached the stage of limited initial commercial use. Newer nonthermal technologies, such as high-pressure, electric-field pulses and pulsed light, promise better retention of nutrients, better retention of sensory attributes such as flavours, natural colours and overall freshness in comparison to old-style heat preservation.

Advances in packaging materials and technology have introduced the possibilities of lighter-weight and thinner-walled containers and laminated films with unique gas transmission that permit better preservation by, e.g., less oxidation. Some packaging materials incorporate antimicrobials that increase shelf life without affecting the composition of the food. New packages deliver excellent protection of the food during its shelf life while offering greater ease of opening to those who might be handicapped or elderly.

Food industries and technologists are constantly seeking better, faster, more environmentally friendly and more economical technologies that deliver improved products. Ever-improving technologies are constant drivers in the evolution of foods, their production and their properties, including nutritional and health attributes. But many hurdles remain to be overcome before any new technology can be widely used. Enormous costs of

development and implementation are associated with any new technology. Such a technology must demonstrate clear superiority and be feasible and cost efficient on a very large scale. It should have achieved general acceptance in the industry, among regulators and, of course, consumers. Although the food industry has good reasons for its conservative approach (which will probably become less so in the future), it will still insist on the highest standards of safety and integrity. And, in the long run, consumers will accept and eat only foods that taste good.

## ***FUTURE PERSPECTIVES***

---

Considerable progress has been made in scientific knowledge leading to identification and characterisation of the functional effects of foods. Good health is closely linked to a healthy lifestyle, specifically to good dietary habits that conform to food guidelines, the established dietary recommendations and the latest nutritional science. Indeed the optimisation of body functions and the development of well-being and good health through a varied diet and the reduction of the risk of developing certain diet-related disorders by means of suitable food choices are major priorities for many interested parties. These include scientists, consumers, governments and food manufacturers.

### ***Improving the substantiation of claims for functional foods***

Future attention will focus on claims for functional foods (Box 5). As mentioned previously, the main thrust of the FUFOSE document was to suggest the outline of a scheme whereby claims for functional foods should be linked to solid scientific evidence and whereby claims for enhanced function and reduced risk of disease are justifiable only when they are based on appropriate and validated markers of exposure, enhanced function or reduction of disease risk (see Figure 2).

The principles and conclusions defined within the FUFOSE document must now be brought to the application stage. A European scientific network (A Process for the Assessment of Scientific Support for Claims on Foods [PASSCLAIM]) was initiated by ILSI Europe in 2001. PASSCLAIM's objective is to produce a consensus on basic principles for assessing the scientific substantiation of claims. The outcome of this EC concerted action will be widely disseminated among the scientific, industrial, regulatory and consumer communities.

## BOX 5

### *Future focus*

Health-related claims should be:

- Scientifically substantiated.
- Valid for the food as it is consumed or in its future anticipated use to reach the minimal effective dose.
- Communicated clearly, understandably and truthfully to the consumer.

Therefore, there is an urgent need to establish guidelines on how to:

- Support the scientific substantiation of such effects as a basis for claims.
- Communicate benefits to consumers and health professionals.

## *Improving communication about functional foods*

Ideally, the communication of health-related claims to the consumer will include any claims made on the package label, advertisements, product information sheets, recipe brochures, marketing brochures, spoken and textual content of video, film and TV commercials and web sites. Claims should trigger nutrition labelling and be truthful, unambiguous and understandable.

The wording should also make clear that the health-related claim applies only to the functional food consumed in the context of a total dietary pattern. It should not encourage over-consumption of a given food product to the detriment of others. It should include information on the quantity of the functional component or ingredient, on the target group or potentially vulnerable segment of the population, if appropriate. It should further mention how to consume or use the functional food to obtain the claimed effect, if relevant. Moreover, the likely consumer perception of the health-

## BOX 6

### *Recommendations for good documentation to substantiate a claim*

Good documentation will:

- Refer to the process of scientific substantiation and its principles.
- Be based on, but not misinterpret or overemphasise, the scientific substantiation.
- Give a clear and truthful summary of the appropriate scientific data.
- Describe how these scientific data supporting the health-related claim were collected and evaluated.
- Explain the plausibility in terms of scientific knowledge.

related claims should be taken into consideration in communications.

Communicating health-related claims also includes producing the documentation that gives the scientific underpinning to the claim. This is usually available as a scientific dossier for health professionals and research scientists (Box 6), but a simplified version for consumers, in the form of a product information sheet that accompanies the product, will always help the communication process.

## **Developments within the European Union**

Several draft documents about claims were produced by the EC at the turn of the 21st century. In June 2002, a Draft Proposal on Nutrition, Functional and Health Claims Made on Foods was issued for consultation. It is expected to be formally adopted as an EC proposal by the end of 2002 and formal negotiations involving Member States are expected to begin early in 2003. In this draft proposal, health claims will include both “enhanced function claims” and “reduction of disease risk factor claims”.

## Codes of Practice for Health Claims in Europe

In January 2000, the EC White Paper on Food Safety noted that “Consumers have the right to expect information on food quality and constituents that is helpful and clearly presented, so that informed choices can be made”. In addition, it stated that “The Commission will consider whether specific provisions should be introduced into EU law to govern ‘functional’ claims”.

Even in the absence of a European legislation, several European countries have instigated self-regulating programmes and codes of practice for health claims. Sweden was the first to introduce such a programme. It allows mention of eight diet-related diseases or risk factors in connection with the relevant nutrient or dietary fibre content of a food product:

- obesity–energy;
- blood cholesterol–SFAs and certain gel-forming types of fibre;
- blood pressure–sodium chloride;
- atherosclerosis–factors affecting blood cholesterol and/or blood pressure and n-3 fatty acids in fish and fish products;
- constipation– dietary fibre;
- osteoporosis–calcium, dental caries–absence of easily fermented carbohydrates; and
- iron deficiency–iron content.

The claims are in two steps: citation of one of these diet and health relationships, followed by a statement on the relevant composition of the product. The Swedish code recently has been extended to include “product-specific” physiological claims, i.e. innovative enhanced function claims based on physiological effects demonstrated in normal consumption of the product.

In the Netherlands, the Dutch Nutrition Centre has drawn up a code for the use of health claims with support from regulatory authorities, industry and

consumer organisations. Belgium, too, has a code of conduct driven mainly by the Federation of Food Industries. In Germany and France, health claims for foods are approved on a case-by-case basis. Denmark is drawing up a list of generic health claims along the lines of the United States and Swedish models. In Finland, the National Food Administration has published guidelines for permissible health claims that are currently being reconsidered. In the United Kingdom, the Joint Health Claims Initiative was launched at the end of 2000 and has produced its first list of generic claims.

These codes all contain guidelines and conditions for the use of health claims. Some encourage companies seeking to make innovative health claims to submit full documentation of the scientific evidence that forms the basis of the claim to an expert panel for guidance and approval.

## Promoting the role of functional foods in the diet alongside the promotion of general healthy eating advice

There need be no conflict between those who promote general healthy eating advice and those who want to develop and promote functional foods. Indeed, the promotion of one should complement the promotion of the other. As our knowledge of diet-gene interactions progresses, some people may be especially motivated to consume certain functional foods in conjunction with a well-balanced diet (Box 3).

The development of functional foods offers great potential for improving health and quality of life for many people. It is essential that the scientific evidence for these products be correctly substantiated before the potential health benefits are widely communicated to the public. This will ensure the credibility of the claimed benefits of the products. The collaboration between the many disciplines involved in food and nutrition science, therefore, is essential for successful and credible innovation in functional food development.

## GLOSSARY

---

**Antioxidant:** Any substance that can delay or prevent oxidation in the presence of oxygen.

**Bioavailability:** Fraction of an ingested nutrient utilised for functional demands in target tissue(s).

**Case control study:** Study design in which persons with a disease (cases) are compared with those without the disease (controls) to see how their exposures to causative factors may have differed.

**CODEX Alimentarius (CA):** Meaning, literally, “food code”, a compilation of standards, codes of practice and recommendations put out by the Codex Alimentarius commission, which meets every 2 years. Membership is open to all countries associated with the Food and Agriculture Organization of the United Nations and with the World Health Organization. The CA has 168 members and covers more than 98% of the world population.

**Cognitive function or ability:** Knowledge, perception.

**Cohort study:** Study design in which data on exposures to possible risk factors for disease are collected from a group of people who do not have the disease under investigation. The subjects are then followed for a period of time to see whether the later development of disease is related to factors that were measured.

**Confounding factors:** Factors that distort an association because they are associated with an exposure as well as a disease or other outcome.

**Diabetes mellitus:** Metabolic disorder in which the hormone insulin is ineffective, either because of failure in its secretion by the pancreas (type 1, insulin-dependent [IDDM] diabetes) or because target tissues are insensitive to its action (type 2, non-insulin-dependent diabetes). In type 1, patients require regular administration of insulin. In contrast, patients with type 2 may actually have a high blood concentration of insulin (hyperinsulinaemia) and the condition is frequently associated with obesity and hyperlipidaemia.

**Dietetic foods:** foodstuffs intended to satisfy particular nutritional requirements of specific groups of the population. See the EU Framework Directive 89/398/EEC and its amendments 96/84/EC and 1999/41/EC.

**Ecological study:** A study that compares rates of exposures and diseases in different populations using aggregate data on exposure and disease, not individual data.

**Enhanced function claims:** Claims that concern specific beneficial effects of foods, nutrients, components or ingredients on physiological, psychological functions or biological activities beyond their established role in growth, development and other normal functions of the body.

**FDA:** The Food and Drug Administration of the United States.

**FOSHU:** (Japan) Foods for Specific Health Use (FOSHU) are required to provide evidence that the final food product is expected to exert a health or physiological effect; data on the effects of isolated individual components are not sufficient. FOSHU products should be in the form of ordinary foods (i.e. not as pills or capsules) and are assumed to have been consumed as part of an ordinary diet (i.e. not as occasional items linked to specific symptoms). Most FOSHU products currently approved contain either oligosaccharides or lactic acid bacteria for promoting intestinal health.

**FUFOSE:** The European Commission Concerted Action on Functional Food Science in Europe.

**Functional food:** A food can be regarded as functional if it is satisfactorily demonstrated to affect one or more target functions in the body beyond adequate nutritional effects, in a way that is relevant either to an improved state of health and well-being and/or the reduction of risk of disease.

**Functional food science:** the study of new concepts in nutrition that lead to research and development of functional foods.

**Generic health claims:** Claims based on a consensus in the scientific community regarding a well-established, generally accepted diet–disease or diet–health relationship.

**GRAS:** “Generally recognised as safe” status.

**Health claim:** A direct, indirect or implied claim in food labelling, advertising and promotion indicating that consumption of a food carries a specific health benefit or reduces the risk of a specific health detriment.

**High-density lipoproteins (HDL):** Plasma lipoproteins containing low concentrations of cholesterol and other lipids; believed to be beneficial.

**Homocysteine:** An amino acid. Epidemiological data suggest that high plasma levels of homocysteine are associated with increased risk of cardiovascular disease.

**Intervention trial:** A study in which exposure to the factor under investigation is modified by the investigator; an experimental study.

**Lipoproteins:** Particles composed of specialised protein and lipids, including triacylglycerol, cholesterol and phospholipid. They enable (water insoluble) lipids to be carried in blood plasma.

**Low-density lipoproteins (LDL):** Plasma lipoproteins containing high concentrations of lipids (low density compared with that of water), including cholesterol. Increased concentrations are a risk factor for coronary heart disease.

**Medicinal claim:** A claim that states or implies that a food has the property of treating, preventing or curing human disease or makes any reference to such a property.

**Micronutrients:** Vitamins and mineral salts (as distinct from macronutrients – fats, carbohydrates and proteins).

**Non-insulin-dependent diabetes mellitus:** See diabetes mellitus.

**Optimal nutrition:** The principle of maximising the quality of the daily diet in terms of nutrient intakes to favour the maintenance of health.

**Plant stanols:** Products of the industrial hydrogenation of sterols.

**Plant sterols:** Natural constituents of plants, including trees, and a number of common crops, such as soy and maize, which provide sources for food use.

**Prebiotic:** A nondigestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or modify the metabolic activity of one or a limited number of bacteria in the colon, that have the potential to improve host health.

**Probiotic:** A live microbial food ingredient that, when ingested in sufficient quantities, exerts health benefits on the consumer.

**Product-specific (or innovative) claims:** Claims that imply that the food product, as such, has certain physiological effects. These claims require demonstration of the claimed effects when the specific food product is consumed in realistic amounts.

**Prospective cohort or follow-up study:** Type of epidemiological study that measures exposure to factors that may affect health in a group of people (cohort) and relates these factors to the onset of disease in time (during follow-up).

**Reactive oxidative species:** These act as oxidants and are believed to be major contributors to ageing and to many of the diseases associated with ageing.

**Reduction of risk of disease claims:** These claims relate to the consumption of a food, a nutrient, a component or an ingredient that might help reduce the risk of a specific disease or condition.

**Substrate metabolism:** A number of chronic diseases such as obesity, type 2 diabetes and osteoporosis are partly related to changes in total food intake, levels of physical activity and a poorly balanced diet. The balance of the diet can determine substrate metabolism, and the optimally balanced diet is usually expressed in terms of its macronutrient content.

**Synbiotic:** A mixture of probiotics plus prebiotics with the aim to increase survival of health-promoting bacteria, with the ultimate goal of modifying the gut flora and its metabolism.

**Target functions:** Biological responses (functions) that play a major role in maintaining an improved state of health and well-being and/or reduction of risk of disease.

## **FURTHER READING**

---

Ashwell, M. (2001). Functional Foods: A Simple Scheme for Establishing the Scientific Basis for all Claims. *Public Health Nutrition*. CABI Publishing, Oxford, UK, 4(3):859–862.

Bellisle, F., Diplock, A.T., Hornstra, G., Koletzko, B., Roberfroid, M.B., *et al.*, eds. (1998). Functional Food Science in Europe. *British Journal of Nutrition*. CABI Publishing, Oxford, UK, 80(Suppl.1):S1–S193.

Codex Alimentarius Commission (1997). Guidelines for Use of Nutrition Claims (CAC/GL 23-1997). *Codex Alimentarius*. FAO/WHO, Rome, Italy, Vol. 1A.

Codex Alimentarius Commission (2002). Proposed Draft Guidelines for Use of Health and Nutrition Claims. *Codex Alimentarius*. FAO/WHO, Rome, Italy, Alinorm 03/22.

Committee of Experts on Nutrition Food Safety and Consumer Health (1999). Ad Hoc Group on Functional Food. Council of Europe, Strasbourg, France.

Confederation of the Food and Drink Industries of the European Union (CIAA) (1999). CIAA Code of Practice on the Use of Health Claims. CIAA, Brussels, Belgium.

Diplock, A.T., Aggett, P.J., Ashwell, M., Bornet, F., Fern, E.B., Roberfroid, M.B., eds. (1999). Scientific Concepts of Functional Foods in Europe: Consensus Document. *British Journal of Nutrition*. CABI Publishing, Oxford, UK, 81(Suppl.):S1–S27.

European Commission (2000). White Paper on Food Safety. European Commission, Brussels, Belgium, COM(1999)719 final.

European Commission, Directorate General SANCO (2002). Draft Proposal for Regulation of the European Parliament and of the Council on Nutrition, Functional and Health Claims Made on Foods. European Commission, Brussels, Belgium, Working document 1832/2002.

ILSI Europe Addition of Nutrients to Food Task Force (1990). Addition of Nutrients to Foods: Nutritional and Safety Considerations. *ILSI Europe Report Series*. ILSI Press, Washington, DC, USA.

ILSI North America Technical Committee on Food Components for Health Promotion (1999). Food Component Report. ILSI Press, Washington, DC, USA.

Knorr, D. (1999). Technology Aspects Related to Microorganisms in Functional Food. *Trends in Food Science and Technology*. Elsevier Science, UK, 9(8-9, Special Issue):295–306.

Langseth, L. (1995). Oxidants, Antioxidants and Disease Prevention. *ILSI Europe Concise Monograph Series*. ILSI Press, Washington, DC, USA.

Langseth, L. (1996). Nutritional Epidemiology: Possibilities and Limitations. *ILSI Europe Concise Monograph Series*. ILSI Press, Washington, DC, USA..

Langseth, L. (1999). Nutrition and Immunity in Man. *ILSI Europe Concise Monograph Series*. ILSI Press, Washington, DC, USA..

Roberfroid, M.B. (2000). Defining Functional Foods. In: Gibson, G. and Williams, C., eds. *Functional Foods*. Woodhead Publishing Ltd., Cambridge, UK.

Truswell, A.S. (1995). Dietary Fat: Some Aspects of Nutrition and Health and Product Development. *ILSI Europe Concise Monograph Series*. ILSI Press, Washington, DC, USA.

US Food and Drug Administration (1999). Guidance for Industry-Significant Scientific Agreement in the Review of Health Claims for Conventional Foods and Dietary Supplements. Food and Drug Administration, Washington, DC.

# Other ILSI Europe Publications

## Concise Monographs

- A Simple Guide to Understanding and Applying the Hazard Analysis Critical Control Point Concept
- Calcium in Nutrition
- Caries Preventive Strategies
- Dietary Fat – Some Aspects of Nutrition and Health and Product Development
- Dietary Fibre
- Food Allergy and Other Adverse Reactions to Food
- Food Biotechnology – An Introduction
- Health Issues Related to Alcohol Consumption
- Healthy Lifestyles – Nutrition and Physical Activity
- Microwave Ovens
- Nutrition and Immunity in Man
- Nutritional and Health Aspects of Sugars – Evaluation of New Findings
- Nutritional Epidemiology, Possibilities and Limitations
- Oxidants, Antioxidants, and Disease Prevention
- Principles of Risk Assessment of Food and Drinking Water Related to Human Health
- Sweetness – The Biological, Behavioural and Social Aspects
- The Acceptable Daily Intake – A Tool for Ensuring Food Safety

## Concise Monograph in preparation

- Carbohydrates: Nutritional and Health Aspects

## To order

ILSI Europe  
83 Avenue E. Mounier, Box 6  
B-1200 Brussels, Belgium  
Phone (+32) 2 771 00 14  
Fax (+32) 2 762 00 44  
E-mail: [publications@ilsieurope.be](mailto:publications@ilsieurope.be)

## Reports

- An Evaluation of the Budget Method for Screening Food Additive Intake
- Applicability of the ADI to Infants and Children
- Approach to the Control of Entero-haemorrhagic *Escherichia coli* (EHEC)
- Assessing and Controlling Industrial Impacts on the Aquatic Environment with Reference to Food Processing
- Assessing Health Risks from Environmental Exposure to Chemicals: The example of drinking water
- Detection Methods for Novel Foods Derived from Genetically Modified Organisms
- Food Safety Management Tools
- Functional Foods – Scientific and Global Perspectives
- Markers of Oxidative Damage and Antioxidant Protection: Current status and relevance to disease
- Method Development in Relation to Regulatory Requirements for the Detection of GMOs in the Food Chain
- Overview of Health Issues Related to Alcohol Consumption
- Overweight and Obesity in European Children and Adolescents: Causes and consequences – prevention and treatment
- Packaging Materials: 1. Polyethylene Terephthalate (PET) for Food Packaging Applications
- Packaging Materials: 2. Polystyrene for Food Packaging Applications
- Packaging Materials: 3. Polypropylene as a Packaging Material for Foods and Beverages
- Recycling of Plastics for Food Contact Use
- Safety Assessment of Viable Genetically Modified Microorganisms Used in Food
- Safety Considerations of DNA in Foods
- *Salmonella* Typhimurium definitive type (DT) 104: A Multi-resistant *Salmonella*
- Significance of Excursions of Intake above the Acceptable Daily Intake (ADI)
- The Safety Assessment of Novel Foods
- Threshold of Toxicological Concern for Chemical Substances Present in the Diet
- Validation and Verification of HACCP



The International Life Sciences Institute (ILSI) is a nonprofit, 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.

ILSI Europe  
Avenue E. Mounier 83, Box 6  
B-1200 Brussels, Belgium  
Phone: (+32) 2 771 00 14  
Fax: (+32) 2 762 00 44  
E-mail: [info@ilsieurope.be](mailto:info@ilsieurope.be)  
Website: <http://europe.ilsii.org>

**ILSI Press**

ISBN 1-57881-145-7



9 781578 811458