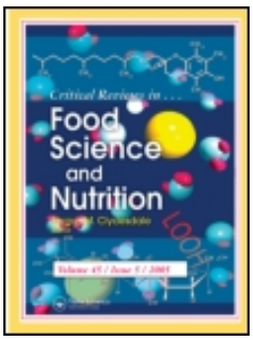

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Health Risks and Adverse Reactions to Functional Foods

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Functional foods have become increasingly popular with consumers anxious to mitigate the effects of an unhealthy lifestyle or aging. In spite of attractive health claims, these products do not have legal or regulatory status in most countries and are regulated through their health claims. Regulation of functional foods by health claims does not address health risks and adverse effects of these products. In this essay regulatory aspects of functional foods are reviewed along with adverse effects published in the peer-reviewed literature. We detail why the lack of an internationally accepted definition of functional foods places consumers at risk of adverse outcomes. Our review will assist regulatory agencies, manufacturers and consumer groups to assess the benefits and reduce the risks associated with these products.

Keywords Functional foods; food allergy; hyperallergenic foods; food regulation; food labels

INTRODUCTION: FUNCTIONAL FOODS-FOODS WITH ADDED HEALTH BENEFITS

Food is a basic necessity to sustain life. The non-nutritional health-promoting benefits of certain foods have been recognized for millennia (Tapsell, 2008). These foods have been termed functional foods. Functional foods claim health benefits above and beyond their nutritional value (Ferguson, 2009). While all foods inherently have beneficial effects on physiological function, functional foods must contain specific ingredients, which improve health or reduce the risk of disease. These ingredients may either be an intrinsic part of the food or may be added (or removed) during manufacture (Henry, 2010).

Functional foods have become increasingly popular with a population anxious to mitigate the effects of either an unhealthy lifestyle or aging (Inzitari, 2011). A mistrust of conventional medicine may partly underlie this popularity (Vranesic-Bender, 2010; Crowe and Francis, 2013). The health benefits claimed by manufacturers of functional foods are an attractive option for affluent consumers in developed countries (de Froidmont-Gortz, 2009). The world market for these products was estimated to be worth over €50 billion in 2009 (Nicoletti, 2012).

Functional foods first appeared in Japan in the 1980s and have subsequently been marketed in other parts of the world including Australasia, the European Union, and North America (Arai, 2001; Ozen, 2014; Ozen et al., 2012).

EXAMPLES OF FUNCTIONAL FOODS

Functional foods may be processed natural foods with identified health promoting ingredients such as oats, which may reduce cardiovascular risk by improving lipid profiles (Williamson, 2009). In other cases specific ingredients are added to improve health outcomes. Examples of the latter category include margarines fortified with omega 3 unsaturated fatty acids, which again may improve lipid profiles and reduce cardiovascular risk (Sirtori, 2009).

Other recent examples of functional foods include *Wh$_2$ole*® where whey proteins have been isolated, concentrated and added to flavoured water to reduce appetite (Ameratunga and Woon, 2010). Consumption of whey proteins has been shown to induce satiety (Luhovyy et al., 2007). In the future, it is likely that an increasing number of functional foods will be manufactured by transgenic technology with the hyper-expression of potentially beneficial genes (Lee and An, 2009; Farhi, 2013).

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Table 1 Some examples of claimed health benefits of functional foods

- Cardiovascular risk reduction: improvement of lipid profile
- Weight, appetite suppression
- Reduced diabetes risk
- Cancer risk reduction
- Reduction in neural tube defects e.g. folate supplementation.

REGULATION OF FUNCTIONAL FOODS

Currently there is no universally accepted definition of functional foods (Henry, 2010). With the possible exception of South Korea and Japan, functional foods do not have a legal or regulatory status.

Functional foods make a beneficial health claim when marketed. Most countries have strict laws governing health claims on packaging. In most countries, health claims and labelling are the de facto mechanisms for regulating functional foods (Serafini et al., 2012).

Health claims are statements that suggest or imply a relationship between consumption of a food or an ingredient and improved health outcomes (Aggett, 2005). Manufacturers of functional foods have made substantial health claims including reducing the risk of cancer, improving cardiovascular risk, improved well-being and appetite suppression (Table 1) (Stark and Madar, 2002). Health claims are a key marketing tool (Vincent van Buul and Fred Brouns, 2013). Consumers often base their decisions to purchase foods on these claims (Mariotti, 2010).

OTHER PRODUCTS WITH ACCLAIMED HEALTH BENEFITS (Fig. 1)

There is considerable overlap between functional foods and other products bearing a health claim (Hasler and Brown, 2009). The level of the health claim will determine how the product is regulated and marketed. A product claiming to reduce the risk of a specific disease will require a robust evidence base compared to one, which makes claims of a more general nature e.g., "a good source of fibre" (Grossklaus, 2009).

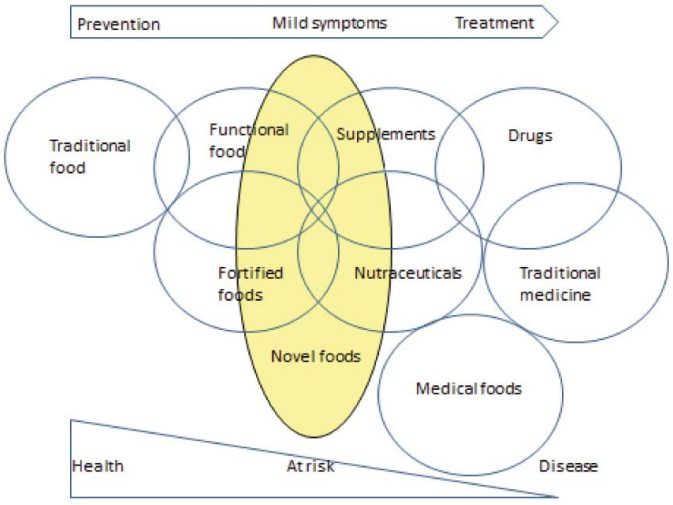

Figure 1 Relationship between functional foods and other products with acclaimed health benefits.

The distinction between functional foods and traditional foods is blurred (Figure 1). In many cases foods may have been consumed over the centuries before a specific health benefit is identified (Stark and Madar, 2002). These foods may then be deemed functional foods. In other cases a specific ingredient has been added to enhance its health promoting effects. The type of health claim will determine the marketing and regulation of these foods (Serafini et al., 2012).

Functional foods overlap with products termed nutraceuticals (nutrient and pharmaceutical) reflecting their claimed health promoting benefits (Eussen, 2011). Some authors make a distinction between functional foods and nutraceuticals, which typically contain added or purified ingredients such as Echinacea. Dr Stephen DeFelice defined nutraceuticals as "Food, or parts of food, that provide medical or health benefits, including the prevention and treatment of disease" (Brower, 1998). Health Canada defines nutraceuticals as products isolated or purified from foods which are sold in medicinal forms not usually associated with food (Hasler and Brown, 2009). Unlike functional foods, nutraceuticals may have a recommended dose per day. Like functional foods, nutraceuticals have no legal or regulatory status (Kalra, 2003).

In contrast, prescription medicines are strictly regulated in most countries. Medicines are marketed to prevent, mitigate or treat a specific disease. These products undergo rigorous evaluation prior to market release. Some may be derived from animal or plant sources. These products are typically monitored long after their release and generally require a written prescription by a registered medical practitioner. Recently some foods with functional ingredients have been allowed a "disease risk reduction" label by the European Food Safety Authority (EFSA) (Mariotti et al., 2010). Such foods have undergone rigorous evaluation and their efficacy has been demonstrated by randomised placebo controlled studies.

Medical foods have been specifically formulated for patients suffering from a disease where conventional foods may be nutritionally inadequate or cause toxicity. Examples include short chain fatty acids for patients suffering from fat malabsorption or amino acid formulas for infants with severe milk allergy (Hill, 2007). These foods are regulated in a similar way to drugs and are usually prescribed by a registered medical practitioner.

Functional foods are also distinguished from dietary supplements. Dietary supplementation helps to meet physiological needs when nutrient intake from the diet is inadequate (Craig, 2010). Some botanical products are also considered supplements (Nicoletti, 2012). Supplements are typically sold in capsule or tablet form. Unlike foods, there is a recommended daily dose. There is however, considerable overlap between

functional foods, nutraceuticals, and dietary supplements (Fig. 1). Some functional ingredients may be available in capsule form or added to foods (Eussen et al., 2011).

In contrast to functional foods, most regulatory authorities have legislation covering novel foods. Most of these novel food laws were primarily designed to cover genetically modified foods (van Putten, 2011). The definition of novel foods is however not consistent across regulatory authorities. Generally, novel foods will fall into one of three categories. They may be genetically engineered, produced by a new process, or may not have a history of consumption in that jurisdiction (van Putten et al., 2011). Functional foods and ingredients may be covered by novel food regulations in some parts of the world.

Fortified foods are created by the deliberate addition of a micronutrient, which may otherwise be deficient in an individual's diet. Iodine supplementation of table salt has prevented iodine deficiency in many parts of the world (Charlton and Skeaff, 2011). In some cases, the addition of an ingredient may reduce the risk of disease as seen with folate supplementation of bread to prevent neural tube defects. Once more there is overlap between fortified foods and functional foods (Fig. 1) (Heseker, 2011).

Functional foods are also to be distinguished from traditional medicine. The World Health Organization (WHO) defines traditional medicine as:

> "the health practices, approaches, knowledge and beliefs incorporating plant, animal and mineral-based medicines, spiritual therapies, manual techniques and exercises, applied singularly or in combination to treat, diagnose and prevent illnesses or maintain well-being".

Some forms of traditional medicine involve herbal treatments (Peltzer, 2009). There may be overlap with Western medicine. An example of this includes the development of Artemesinin from the plant *Artemisia annua* L, as an effective treatment for malaria (Tu, 2011).

For the purposes of this review, we have defined functional foods as products that are consumed as part of the normal diet, which have additional health promoting or disease preventing properties. This is similar to the definition used by Health Canada (Henry, 2010). Given the lack of an universally accepted definition (Crowe and Francis, 2013), it is likely there will be significant overlap between functional foods and other products including traditional foods, novel foods, nutraceuticals, fortified foods, supplements, and traditional medicines (Fig. 1) (Hasler and Brown, 2009).

REGULATION OF HEALTH CLAIMS

There are a number of regulatory agencies responsible for the development of food standards internationally. The Codex Alimentarius Commission (Codex) was established by the WHO and the Food and Agriculture Organization (FAO) for the international harmonisation of food standards for consumer protection (Somogyi, 2011). Codex publishes codes of conduct for the food industry to ensure safe and fair trading practices (Randell and Whitehead, 1997).

Codex is developing guidelines for the use of nutrition and health claims based on the strength of scientific evidence (Grossklaus, 2009). The proposed assessment criteria are similar to the rigorous criteria used to judge the efficacy of a drug or other medical intervention. Randomised controlled intervention studies are given the highest status (level 1 evidence) while case studies are given the least credibility.

Similarly, other food safety organisations have begun assessing the evidence base for health claims. The EFSA has strict criteria for accepting health claims on foods (Asp and Bryngelsson, 2008). As part of the application for a health claim, scientific evidence **(regulation 1924/2006)** must be provided for a beneficial physiological effect. The ingredients subject to a health claim must be clearly identified and be available in a sufficient quantity for regular consumption.

Health claims have also been addressed by the International Life Sciences Institute Europe (ILSI) and two frameworks have been developed to assess health claims and therefore functional foods. The Functional Food Science in Europe (FUFOSE) project established the framework for evaluating the effect of the food/ingredient on the individual and developed biomarkers, which were consistent with the desired effect (Aggett, 2009). The Process for the assessment of Scientific Claims on Foods (PASSCLAIM) project established the methodology for reviewing the evidence base for the claim. The highest level of evidence is given to randomized control trials while in vitro data and animal studies are given less emphasis (Aggett et al., 2005).

The United States Food and Drug Administration (USFDA) does not have a legal definition of functional foods (Crowe and Francis, 2013). Like most countries these products are controlled by health claims and labelling regulations. The vendor can market products as conventional foods, food additives, dietary supplements, medical foods, or food for special dietary use. The intended use determines the relevant regulatory framework applied to the product (Lupton, 2009).

The American Dietetic Association (ADA) has classified the evidence for health claims varying from very strong to weak (Hasler and Brown, 2009). The ADA does not have a regulatory role in the approval or registration of health claims for foods.

HEALTH RISKS ASSOCIATED WITH FUNCTIONAL FOODS (Table 2)

Risks of Inaccurate Health Claims:

Closer scrutiny of many of these health claims is problematic. Often the benefit is modest and requires that the product

Table 2 Risks associated with functional foods Consequences

Risks associated with inconsistent definition	regulatory inconsistencies
Risks of regulatory inconsistencies	consumer confusion
Risk of poor quality control	poor efficacy or toxic effects
Risk of carcinogenicity	cancer
Risk of adverse reactions to functional foods	allergy, toxicity etc (Figure 2)

is consumed on a regular basis (Hasler and Brown, 2009). The benefits may not be apparent for a considerable period and may need large, long-term studies to demonstrate efficacy (AbuMweis et al., 2010). A reduction in coronary artery disease may not be apparent for several years but it is accepted that surrogate markers for risk reduction (lipid profiles, CRP levels, etc.) may be identified in short term randomised studies (Chen, 2014; Massaro, 2010). The FUFOSE framework established the validity of using biomarkers to confirm a beneficial effect (Aggett, 2009).

The benefits of functional foods may be confounded by other lifestyle or genetic factors. Moreover, consumption of other foods also has the potential to confound observations.

In many cases, the active ingredients of functional foods may not be obvious. The active components of the functional food have the potential to interact with the food matrix, which may alter their bioavailability (Sensoy, 2014).

Many functional foods have been tested in animals or in vitro (Kim et al., 2009). These observations may or may not be relevant for humans. These studies are given the least value by regulatory authorities (Grossklaus, 2009). It is however accepted that some forms of toxicity such as mutagenicity and carcinogenicity are best assessed in animals or by in vitro studies.

Concern has been expressed that exaggerated or fraudulent claims could discredit the food industry and may prevent consumers from purchasing foods, which are genuinely healthful (Jacobson and Silverglade, 1999). Consumers who are sceptical about food claims may become more cynical if exaggerated or fraudulent claims become publicised (Jacobson et al., 2000).

HEALTH RISKS RESULTING FROM POOR QUALITY CONTROL

There is concern about the quality control of functional foods (Sanzini, 2011). Popular functional ingredients include plant extracts such as St. John's wort, echinacea, Ginkgo biloba, saw palmetto, and ginseng. Dosages are not standardized and the source and plant components may not be identified by the manufacturer. There is no USFDA standard to ensure that the functional ingredient content in the bottle is reflected on the label. Cases of vitamin D intoxication have resulted from manufacturing and labelling errors (Araki, 2011). There may be batch-to-batch variation in the levels of active components.

The problem is illustrated by several publications where concentrations of Ginko biloba on the label significantly overestimate the content in the bottle. Of more concern was the high concentration of a possible allergen, ginkgolic acid in some preparations (Kressmann et al., 2002). Another recent study found similar problems with Gingko preparations in Poland. Again, high concentrations of gingkolic acid were identified in some products (Gawron-Gzella, 2010).

There is also the risk that closely related herbs and other plants may not be correctly identified during manufacture. This could result either in lack of efficacy or toxicity (Nicoletti, 2012). New analytical techniques such as Phytochemistry and High Performance Thin Layer Chromatography will play a critical role in composition analysis of these products (Nicoletti, 2012). Poor quality control may result in a loss of consumer confidence in products because of a lack of efficacy or increased risk of toxic reactions from over dosage (Ekor, 2014). Detailed quality assurance studies are likely to add to the expense of the product.

In contrast, one of the best examples of an efficacious functional food is oats produced by the Qaker Oats Company. There is convincing data that β-glucan in oats can reduce serum cholesterol. The company showed that 3g of β-glucan could result in a 5% reduction in cholesterol. This evidence was based on multiple clinical studies. After review, the USFDA determined that a food label bearing a cholesterol lowering claim must contain 13 g of oat bran or 20 g oatmeal, and have at least 1.0 g of β-glucan per standard serving (Hasler, 1998). The USFDA granted approval for lipid-lowering labelling based on convincing scientific evidence.

RISKS OF ADVERSE REACTIONS TO FUNCTIONAL FOODS

All foods can cause adverse reactions. We suggest that adverse reactions to functional foods are classified in the same way as adverse reactions to conventional foods (Fig. 2). In the

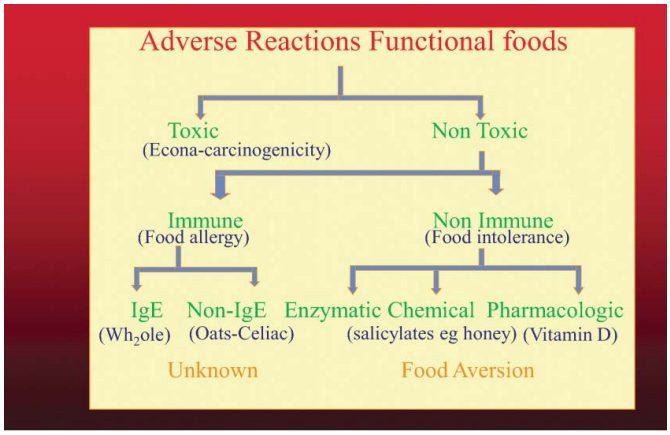

Figure 2 Adverse effects of functional foods—a classification.

case of functional foods, the reactions may occur to the food or to added or enhanced ingredients. If a consumer reacts to the food component of the functional food, they would also be expected to react to the conventional equivalent food. If a consumer reacts to the functional food but not the conventional food, this suggests a reaction to the added ingredient. Distinguishing which component caused the reaction may not be easy.

Reactions to added ingredients can be toxic or non-toxic. Toxic reactions include carcinogenicity. The potential carcinogenicity of Econa oil is described below.

Pharmacological adverse reactions may occur where ingredients are consumed in higher than normal amounts. There is concern that the consumption of large amounts of fish oil may increase the risk of haemorrhage (Komaroff, 2009). However, this has not been supported in a previous review (Harris, 2007).

Of more concern have been reports of chronic toxicity to vitamin D supplements. Consumers may be at risk of life threatening hypercalcemia if they consume food supplements with high concentrations of vitamin D (Lowe, 2011; Kaptein, 2010).

Non-toxic adverse reactions to foods can be due either to intolerance or allergy. Chemical intolerance may occur where some consumers may be susceptible to pharmacological effects of these foods. High concentrations of salicylates in honey for example could trigger respiratory or gastrointestinal adverse effects in susceptible persons (Fig. 2) (Fernando and Clarke, 2009). Safety concerns have been raised about some functional foods containing medicinal herbs. These have the potential to cause pharmacological effects and could interact with prescription medicines (Brazier and Levine, 2003; Ulbricht, 2008).

Risk of Allergic Reactions

Allergic reactions are mediated by the immune system. They can be divided into immediate reactions, usually triggered by IgE (type 1 reactions) or delayed reactions mediated by other arms of the immune system. Type 1 allergic reactions should be tested with a panel of food allergens including the conventional equivalent to the functional food. This may involve skin testing as well as specific IgE testing.

Testing for some types of delayed reactions may involve food patch testing. Examples of delayed food allergy reactions (Fig. 2) include celiac disease aggravated in a subgroup of patients by functional foods containing oats (Pulido, 2009). Celiac disease is considered a delayed food hypersensitivity to gluten, which triggers an autoimmune reaction in susceptible persons (Husby, 2012). Diagnosis requires serological tests for antibodies to tissue transglutaminase or deamidated gliadin peptide followed by an intestinal biopsy (Hope, 2013).

We have recently described severe allergic reactions to a new functional food *Wh$_2$ole*® (Ameratunga and Woon, 2010). Two children suffered anaphylaxis to *Wh$_2$ole*®. A smaller amount of *Wh$_2$ole*® appeared to provoke a more severe reaction in these children than previous reactions to larger amounts of milk formula. Our investigations confirmed that this product contained higher concentrations of β-lactoglobulin in comparison to bovine milk.

The product was sold as an appetite suppressant. Consumption of whey protein has been shown to induce satiety (Luhovyy et al., 2007). After detailed laboratory analysis we determined this product had 10 g/L β-lactoglobulin, which is more than twice the concentration of β-lactoglobulin in bovine milk. We have termed this product a manufactured hyperallergenic food as it has a higher concentration of allergen compared to its food of origin (bovine milk). We had predicted the production of hyperallergenic foods by the food industry (Crooks, 2008).

If an IgE mediated reaction is suspected, skin testing with the functional food should be undertaken. This may need to be performed with caution as the functional food may have a higher concentration of allergen, which could provoke a systemic allergic reaction during testing. Double blind placebo controlled food challenges are the gold standard for diagnosing food allergy but again carry considerable risk if there are high concentrations of allergen in the functional food.

Other Examples of Risk of Allergy to Functional Foods

The addition of fish proteins to experimental ice creams was recently described in Iceland (Shaviklo, 2011). Persons allergic to fish are at risk of severe reactions to these products. Ice creams have previously not contained fish proteins and fish allergic consumers may be at risk if they inadvertently consume such products.

In New Zealand, honey containing bee venom has caused anaphylaxis in Hymenoptera allergic patients (van Putten et al., 2011). Bee venom was added to honey as a treatment for arthritis. This product recently failed the food safety approval process in the United Kingdom. Similarly, the health promoting effects of kiwifruit have been described (Stonehouse, 2013) although severe allergic reactions have been described in some consumers.

Risk of Carcinogenicity

Of serious concern was the Econa fiasco in Japan in 2009, which resulted in hundreds of millions of dollars' worth of oil, being withdrawn due to the potential carcinogenicity of glycidol fatty acid esters (Liao, 2003). Several in vitro and animal studies had raised concern about the carcinogenic potential of di acyl glycerol based fatty acids (Irwin, 1996).

Functional foods can sometimes have paradoxical effects on different segments of the same population. Folate supplementation has been shown conclusively to reduce the risk of neural tube birth defects (Heseker, 2011). Yet, there is evidence suggesting folate can increase the risk of cancer in older persons (Lucock and Yates, 2009). These potential adverse effects highlight the need for continued surveillance of new foods.

Other Health Risks of Functional Foods

Consumers who believe functional foods can compensate for the lack of a healthy, balanced diet may be at nutritional risk. Similarly, consumption of functional foods does not absolve consumers from the responsibility to modify unhealthy lifestyle factors to reduce the risk of degenerative disease (Mariotti et al., 2010).

DISCUSSION: MITIGATING THE RISKS OF FUNCTIONAL FOODS

Although functional foods have entered the market, many aspects of their production, regulation and risks have not been addressed. It is important for regulatory authorities to develop an uniform definition of a functional food. Failure to do so will run the risk of regulatory inconsistencies and difficulties for food manufacturers who export their products to other countries. This also has the potential to cause confusion among consumers who travel to different countries.

In contrast, many regulatory authorities are moving towards a common goal of assessing health claims (Tapsell, 2008; Grossklaus, 2009; Aggett, 2009; Lupton, 2009; L'Abbe, 2008). The more critical the health claim, the more stringent the evidence base for approval. Foods claiming disease risk reduction will require the highest level of evidence based on multiple randomised controlled studies. The Qaker Oats Company has shown that health claims can be supported by robust scientific data. In other cases, the lack of clinical studies and inconsistent quality assurance makes assessment difficult.

As suggested by Codex, regulatory authorities should classify the strength of evidence for health claims using a verbal scale from weak to conclusive (Grossklaus, 2009). Each rating should be specific for an individual product. This is similar to the ADA classification (Hasler and Brown, 2009). This approach will allow consumers to make an informed choice.

Periodic re-evaluation of health claims on food labelling has been suggested by Codex (Grossklaus, 2009). The strength of the claim could increase with the provision of new data. This would encourage ongoing research as there will be commercial advantages to manufacturers. Consumers will have confidence that health claims have been carefully reviewed by regulatory authorities in their jurisdiction. This will also add to the credibility of the regulatory authority.

We accept that progress has been made towards global harmonisation of health claims. However, regulating these products through health claims will not address the concerns raised in this article including quality control and health risks. Regulation of functional foods through health claims should therefore be regarded as an interim measure. In the longer term, regulatory authorities must develop a consistent regulatory approach to functional foods.

Allergen risk assessment should be an essential part of the pre-market safety and risk analysis for functional foods. While many authorities require allergen assessment for novel foods, the precise methods are not specified. Not all functional foods are considered novel foods and may be exempt from allergen risk assessment (van Putten et al., 2011).

Allergic patients are at risk of severe reactions if they accidentally consume foods to which they are hypersensitive. Avoidance of inadvertent consumption of allergenic products is the joint responsibility of manufacturers, regulatory authorities and allergic consumers. Most patients with food allergies are vigilant about allergen avoidance. Labelling is a critical part of allergy risk reduction. Manufacturers have a legal responsibility to clearly label their products if they contain well-recognised allergens. Where a product has not previously contained an added allergen e.g., ice cream with fish proteins, local labelling, and regulatory requirements may need to be exceeded in order to reduce the risk of inadvertent consumption by an allergic individual.

It is also important for the product name to reflect the nature of the contents. Marketing departments will need to ensure that the name reflects the presence of potential allergens. This is an essential part of risk reduction. We strongly encourage premarket consultation with allergy consumer organisations such as Food Allergy and Anaphylaxis Network in the United States or Allergy New Zealand. This will further reduce the risk of inadvertent consumption by allergic consumers.

We recommend that in vitro and in vivo allergy studies should be undertaken as part of the risk assessment of functional foods, especially if a known allergen has been added. If it is deemed that adding a protein that is a known allergen is necessary to enhance the product, it might be possible to denature the allergen to mitigate the risk to allergic consumers. We have developed immunocap inhibition studies, which could be used to monitor the allergenicity of the protein (Ameratunga and Woon, 2010). Once allergens are denatured, there may be a role for careful quantitative skin testing or even food challenges once appropriate ethics approval and informed consent are obtained. This could be part of the premarketing allergen risk assessment of such products.

Quality control is a critical part of drug manufacture and plays a major role in the consistency of functional foods. Manufacturers and regulatory authorities will need to agree on optimal methods for assessing the quantity and quality of health promoting ingredients in functional foods.

Post market surveillance by regulatory authorities is essential for functional foods. This would allow early identification

of adverse reactions including allergic reactions or toxicity. This may allow early intervention to mitigate the risk including new warning labels on packaging or in extreme cases market withdrawal.

Until there is international agreement on the definition of a functional food, there will continue to be inconsistent approaches by regulatory authorities and consumers will remain at risk. In addition to an internationally accepted definition of functional foods, attention to the scientific validity of health claims, review of the potential for adverse reactions (including allergy) and appropriate labelling will substantially mitigate the risk to consumers. Ongoing postmarket surveillance by the regulatory authority and manufacturer should be mandatory for functional foods.

Investment in strategies to mitigate the risks from functional foods is particularly important for countries such as New Zealand, which are heavily reliant on the export of primary produce. Inadvertent production of highly allergenic foods could damage New Zealand's reputation as a purveyor of high quality foods (Crooks et al., 2008).

AUTHORS CONTRIBUTIONS

RA—conceived the idea of the adverse reactions to functional foods and wrote the first draft

CC—Is nutrition scientist.

GS—contributed to the work of Codex

S-TW—Performed the laboratory work for hyperallergenic functional foods discussed in this article.

Authors have not declared a conflict of interest.

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