Institute of Food Science & Technology

Food Allergy

The Institute of Food Science & Technology has authorised the following Information Statement, dated 24 February 2009, which cancels and replaces any previous versions.

SUMMARY

The problem of food allergens is part of a wider problem, that of all kinds of adverse reactions to foods, which can also result from microbial and chemical food poisoning, psychological aversions and specific non-allergenic responses.

Food allergy is now recognised as an important food safety issue. Dealing with at least the major serious food allergens is an essential part of Good Manufacturing Practice.
The greatest care must be taken by food manufacturers

- ***to formulate foods so as to avoid, wherever possible, inclusion of unnecessary major allergens as ingredients;***
- ***to organise raw material supplies, production, production schedules and cleaning procedures so as to prevent cross-contact of products by "foreign" allergens;***
- ***to train all personnel in an understanding of necessary measures and the reasons for them;***
- ***to comply with the relevant labelling legislation providing appropriate warning, to potential purchasers, of the presence of a major allergen in a product;***
- ***to have in place an appropriate system for recall of any product found to contain a major allergen not indicated on the label warning.***

The purpose of this statement is to describe the nature and cause of food allergies, to outline recent changes in legislation that aim to help allergic consumers to live with their condition and to emphasise the measures that manufacturers and caterers should take to minimise the problems.

BACKGROUND

Adverse reactions to foods

Adverse reactions to foods include not only food allergies but may also result from microbial and chemical food poisoning, psychological aversions, and specific non-allergic responses.

What are food allergy and food intolerance and why are they a problem?

Adverse reactions to food that have an immunological basis are termed ‘food allergies’ and include those which involve immunoglobulin E (IgE)-mediated reactions and the gluten intolerance syndrome, Coeliac disease, which is thought to have a cellular immune mechanism. The macromolecules (usually proteins) involved in sensitising and eliciting such allergic reactions are termed ‘allergens’. In contrast, the term ‘food intolerance’ is used to describe reactions that do not involve the immune system, and includes reactions to histamines and other amines found in foods, and lactose intolerance, where individuals lack

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the enzyme necessary to break lactose down in the gut. Such adverse reactions to foods which lack an immunological mechanism can also be referred to as non-allergic food hypersensitivity reactions.
At present there is no cure for food allergies or food intolerance conditions and, as a result, sufferers have to avoid eating problem foods, or, in some individuals with severe forms of these conditions, any traces of them. Some tragic instances of accidental consumption of allergenic foods, (including so-called "hidden" allergens which have not been declared on food labels) have occurred causing severe, and even fatal, reactions. Avoidance of allergenic foods can be difficult for the allergic consumer and their families/carers, making shopping a time-consuming process as they check food labels. Markets and stalls where foods are sold loose also present problems if utensils used, for example, to serve nut-containing confectionery, are then used for nut-free products. Problems also occur in catering, where dishes are presented without detailed provision of ingredients information, and where in a busy kitchen the same utensils may be used for different foods.

The purpose of this statement is to describe the nature and cause of food allergies, to outline recent changes in legislation that aim to help allergic consumers to live with their condition and to emphasise the measures that manufacturers and caterers should take to minimise the problems.

IgE-mediated food allergies

The immune system produces several different types of molecules known as immunoglobulins, as part of the body's defence mechanism against viral, microbial and fungal infections. One particular form, immunoglobulin E (IgE), is also produced in response to parasitic infections such as the malaria parasite. Sometimes the body can also mount an IgE response towards agents such as pollen, dust, and food, and it is these responses that give rise to allergy syndromes such as hay fever.

IgE-mediated allergies develop in two stages:

1. The first stage is known as sensitisation and occurs when an antigen (almost always a protein) is taken up by cells, known as progenitor B-lymphocytes, capable of maturing into antibody-producing cells. These cells break down antigens and the resulting peptide fragments become bound selectively in the polymorphic groove of major histocompatibility complex (MHC) class II molecules and transported to the cell surface. The complex of "foreign peptide plus self MHC molecule" on the surface of the B-lymphocytes is recognised by the T-cell receptors of $CD4^+$ T helper cells, (another type of immune cell). This event triggers many other changes, including maturation of the B-cells such that they can secrete antibody. As part of 'normal' functioning the body produces IgG and IgA to food proteins, but in certain predisposed individuals, the resulting immune response may take the form of a so-called Th2 response leading to specific IgE production. This type of antibody is normally only produced in response to parasitic infections such as malaria.

2. Stage 2 involves the elicitation of an allergic reaction. IgE becomes associated with specific IgE receptors on the surface of basophil or mast cells, which are packed full of inflammatory mediators such as histamine. On re-exposure to the sensitising agent the cell-bound IgE becomes cross-linked by the agent, causing the mast cells to release the inflammatory mediators. These mediators then trigger the physiological changes that manifest themselves as the symptoms of an allergic reaction. They usually occur quite rapidly (within minutes) following exposure to an allergen and are

quite varied and including respiratory (e.g. asthma), gastrointestinal (e.g. vomiting) and skin (e.g. eczema and hives (nettle rash)) reactions.

Although allergy to peanut, tree nuts and seafood is likely to continue throughout the individual's life, sensitivity to most other allergens is lost in late childhood. This explains the otherwise mystifying estimate that four per cent of adults and eight per cent of children in the EU population suffer from food allergies.

Initial sensitisation has long been the accepted principle, which, *inter alia*, has been the basis for advice to pregnant and breast-feeding women with a family history of peanut allergy to avoid consuming peanuts (advice which in practice has sometimes been mistakenly interpreted as applying to all pregnant women). The basis of this advice has been reviewed by the UK Committee on Toxicity (COT) http://cot.food.gov.uk/pdfs/cotstatement200807peanut.pdf (December 2008). The shift in the balance of evidence since 1998 is such that the Committee believes that the previous precautionary advice to avoid peanut consumption during pregnancy, breast feeding and infancy, where there is atopy or atopic disease in family members, is no longer appropriate. However, the Committee considers that the basis of its more general recommendations made in 1998 is still justified and, therefore, recommends that:

(i) In common with the advice given for all children, infants with a parent or sibling with an atopic disease should be breast-fed exclusively for around 6 months;
and,
(ii) Infants and children who are allergic to peanuts or peanut products, should not consume them or foods that contain them;
and also recommends that:
(iii) those who are allergic to peanut should seek advice from medical professionals about avoidance strategies.

In consequence the UK Food Standards Agency has recommended to Government that the advice be revised in line with the COT recommendations.

Researchers are now carrying out food allergy desensitisation studies to determine whether feeding small amounts of a food allergen to children with a history of allergic reaction to that food could build up tolerance and eventually result in loss of their allergy. The technique, designated oral immunotherapy (OIT), is considered to work on a cellular level to alter the specific response of white blood cells (lymphocytes) that play a part in the immune response during allergic reactions. Studies with egg have shown preliminary promise (Buchanan et al, 2007) and a similar study is proceeding with peanuts (coFAR, 2006). Prof. Gideon Lack, of King's College London, is currently working on novel immunomodulatory treatments for food allergies, and on developing new strategies to prevent food allergies in childhood. He has enrolled more than 200 babies under one year old with eczema or egg allergies in a trial that involves giving half the babies a peanut-containing snack; the other half avoiding peanuts. He will then follow them all until age 5 to see if he has stopped a peanut allergy before it takes hold.

Meanwhile, Dr Andrew Clark and colleagues at Addenbrooke's Hospital, Cambridge, reported a study (Clark AT et al, 2009) in which they investigated if peanut OIT could induce clinical tolerance to peanut protein. They exposed four peanut-allergic children, aged between 9 and 13, to gradually increasing quantities of peanut protein, and found that all the children can now tolerate about 800 mg grams of protein, which is the equivalent to five peanuts, per day. An initial challenge confirmed the presence of peanut allergy in the children, with one of them experiencing anaphylaxis that required an injection of adrenaline.

These initial tests revealed dose thresholds ranging from five to 50 mg, which is the equivalent to between 0.025 and 0.25 of a peanut. The children then began OIT with daily doses of peanut flour. The doses increased fortnightly from 5 to 800 mg of protein. Six weeks later, the oral challenge was repeated, and the new dose threshold values calculated. At the same time, subjects continued daily treatment. During the post intervention challenges, the four children were found to tolerate at least 10 whole peanuts, or 2.4 grams of protein. This equated to a dose threshold increase of 48-, 49-, 55- and 478-fold for the four subjects. Each subject is currently tolerating approximately 800 mg protein (five peanuts) per day, and can tolerate at least double that amount on oral challenge. The result of this study will need to be confirmed in larger studies. Also, tolerance may be lost if subjects were to stop OIT at this stage, and it is likely that long-term maintenance is required, as for other forms of immunotherapy. Follow-up studies are therefore required to examine the duration and frequency of maintenance therapy required to induce long-term tolerance.

OIT should be carried out only under strict medical supervision. Parents are warned not to attempt OIT themselves.

Repeat exposure is because either the person is unaware of being allergic to a particular substance or is aware but unaware of the presence of that substance.

Allergens are usually proteins; other macromolecules such as polysaccharides, can act as allergens, but as these usually only generate poor antibody responses, they are not generally involved in IgE-mediated food allergies. Sensitisation towards many food allergens, such as egg, probably occurs via the gastro-intestinal tract. In adults the onset of food allergy may be related to inhalant allergies such as birch, grass pollen and latex. There is recent evidence to suggest that the dermal route of exposure may also be relevant. As a consequence of homologies between the allergens in, for example, pollen or latex and various fruits and vegetables, such individuals can develop cross-reactive allergies to fresh fruits and vegetables, known as pollen-fruit and latex-fruit syndromes.

Allergic reactions may be triggered by minute amounts of allergen and may range from relatively short-lived discomfort to anaphylactic shock and death (and not only from the well-publicised peanut).

What is the size of the food allergy problem?

Currently good quality information on the prevalence and patterns of food allergy is lacking. About 1-2% of adults and between 5-7% of children is thought to suffer from some type of IgE-mediated food allergy. The higher incidence of allergies in infants is due to allergy to cow's milk, which the children generally grow out of by school age. Estimates of prevalence are complicated by the fact that individuals can develop IgE responses (i.e. be sensitised to an allergen) without that allergen causing an allergic reaction. For example, many patients allergic to peanuts have IgE that can cross-react with soya proteins, but generally they suffer no allergic reaction when they eat soya-containing foods (Eigenmann *et al.,* 1996). This has meant that the "gold standard" for food allergy diagnosis is the double-blind placebo-controlled food challenge, where individuals are given the offending food in increasing doses until objective symptoms of an allergic reaction are observed (Asero et al, 2007; Nørhede, 2007).

Which foods are most often involved in triggering allergies?

Only about eight types of food are thought to be responsible for causing the majority of food allergies, including foods such as cow's milk, egg, fish and shellfish, peanuts, tree nuts,

wheat, and soya (Bush and Hefle 1996). A brief summary of the major allergens in these foods is given in Table 1, together with the allergen names designated by the Allergen Nomenclature sub-committee of the International Union of Immunological Societies. Allergens included in this listing must induce IgE-mediated (atopic) allergy in humans with a prevalence of IgE reactivity above 5%. An allergen is termed major if it is recognised by IgE from at least 50% of a cohort of allergic individuals but does not carry any connotation of allergenic potency; allergens are otherwise termed "minor". The allergen designation is then based on the Latin name of the species from which it originates and is composed of the first three letters of the genus, followed by the first letter of the species finishing with an arabic number e.g. Ara h 1 relates to an allergen from *Arachis hypogea* (peanuts). More detailed information on allergenic foods can be found in the InformAll database http://foodallergens.ifr.ac.uk/

TABLE 1: MAJOR ALLERGENIC FOODS

Food		Major Allergens	Allergen Designation
Cow's milk	Allergens are found in both the whey and casein fractions, although other IgE-reactive proteins have been identified. Cow's milk allergy is predominantly an allergy of infancy and is generally outgrown by school age. It can cause severe reactions and there are reports of just a drop of milk being sufficient to trigger an anaphylactic reaction. Due to the similarity in the protein sequences of caseins and whey proteins from individuals with cow's milk allergy cannot usually tolerate dairy foods based on sheep's and goat's milk. The allergenicity of milk cannot be removed by simple thermal processing.	Casein β-lactoglobulin α-lactalbumin	Bos d 8 Bos d 5 Bos d 4
Hen's Egg	Egg allergy is more frequent in infants many of whom outgrow their allergy by school age. Major allergens originate primarily from egg-white, and include ovomucoid and ovalbumin, which constitute 10% and 50% of egg-white proteins respectively. Both proteins are heavily glycosylated with 25% of the mass of ovomucoid comprising carbohydrate. They are also resistant to enzymatic digestion and denaturation. There are other minor allergens in egg white and yolk. In general, cooking, such as boiling to completely solidify the egg, reduces its allergenic activity. In some instances people who keep birds as pets may develop allergies to their pets, which can sometimes result in allergies to eggs when eaten.	Ovomucoid Ovalbumin	Gal d 1 Gal d 2
Fish	The major fish allergen is parvalbumin a protein which is conserved across fish species. This similarity is responsible for the cross-reactive nature of allergens in cod, salmon, mackerel, herring and plaice, amongst many other fish species. Like other calcium-binding proteins is heat-stable, with the holo-form being both more IgE-reactive and more heat stable than the apo form. As a consequence individuals with fish allergy cannot consume even well cooked fish.	Parvalbumin	Gad c 1 (cod) Sal s 1 (Altlantic salmon)
Shell-fish	Tropomyosin, a heat-stable muscle protein, is the major	Tropomyosin	Pen i 1

and seafood	allergen in shell-fish and seafood, with highly homologous proteins being found in the commonly edible crustaceans. These homologies are responsible for the cross-reactive allergies observed between various types of seafood including shrimps, lobsters, crab, squib and abalone, and inhalant insect allergens, such as those from cockroaches. In addition to being stable to cooking, the allergen leaches from shellfish and seafood into cooking water.		(*Penaeus aztecus)* and similar allergens from other shrimp species including *Penaeus indicus, Penaeus monodon* and *Metapenaeus ensis*
Peanut	Peanut allergy has apparently increased in the last 20 years, particularly in Western countries and appears to be responsible for triggering a greater proportion of severe, life-threatening reactions. Thermal processing (including roasting) does not destroy its allergenic activity although boiling may reduce allergenicity as a consequence of allergens leaching into the cooking water. There do not appear to be significant differences in allergenic properties between different varieties of peanuts. Research has shown that peanut oil (including "refined" peanut oil but not "highly refined" peanut oil).can cause allergic reaction.	7S seed storage globulin 11S seed storage globulins 2S albumin	Ara h 1 Ara h 3,4 Ara h 2, 6, 7
Soya	Whilst allergy to soya is perceived to be a major problem there are many fewer reports of it in the literature than exist for peanut. The allergens include the seed storage globulins and a homologue (Gly m 4) of the major birch pollen allergen, Bet v 1, which appears to be stable to processing procedures as it can be found in textured soya protein although not in roasted beans or fermented products such as soy sauce. In the USA populations with soya allergy have been reported that react to a protein related to a family of proteases, although its sequence has been modified and it has lost its enzymatic activity.	7S seed storage globulin 11S seed storage globulins Bet v 1 homologue Inactive papain-related thiol protease	 Gly m 4 Gly m Bd 30K
Tree nuts Almond Brazil nut Cashew nut Hazelnut Macadamia Pecan Pistachio	Many tree nuts have been described as triggering food allergies, the best studied being hazelnut, Brazil nut and walnut. The major allergens are the seed storage proteins including both the 2S albumins and the 7S and 11/12S globulins. For some nuts, such as hazelnut, allergy can be associated with prior sensitisation to birch pollen, whilst in others (hazelnut, walnut) the non specific lipid transfer proteins are found as allergens. Whilst hazelnut allergies are well characterised, those to other nuts, such as Macadamia, are poorly characterised in the literature although they are included in Annex IIIa of the labelling directive.	2S albumin 7S storage globulins 11S seed storage globulins	Almond Ber e 1 (Brazil nut) Jug r 1 (Walnut), Ana o 3 (Cashew) Jug r 2, Major Almond Protein Ana o 1 (cashew) Cor a 11 (hazelnut),

Queensland Walnut		Non specific lipid transfer proteins Bet v 1 homologue	Ber e 2 (Brazil nut) Ana o 2 (cashew) Cor a 9 (hazelnut) Cor a 8 (hazelnut) Jug r 3 (walnut) Cor a 1.0401(Hazel nut)
Seeds Mustard Sesame	Mustard allergy has been reported in France amongst children, whilst sesame seed allergy is especially important in countries such as Israel, where a sesame-based weaninig food, tahini, is widely used. The major allergens in both sesame and mustard belong to the seed storage proteins and are remarkably stable to processing and proteolysis. Consequently the allergenicity of the foods is unlikely to be modified by thermal processing although there are no studies reporting its impact.	2S albumin	Bra j 1 and Sin a 1 (Mustard) Ses i 1, Ses i 2 (Sesame seeds)
Cereals Wheat	Wheat, barley and rye, contain a range of allergens including the prolamins (alcohol-soluble storage proteins), which are responsible for triggering Coeliac diseases and food allergies such as food-dependent exercise -induced anaphylaxis and atopic dermatitis. Cereals have been found to trigger two types of allergic disease, the occupational allergy known as Baker's asthma, which results from inhalation of flour particles in dusty working environments such as bakeries, and as a consequence of ingestion of cereal containing foods. As a consequence of the similarity of cereal storage proteins individuals with either Coeliac disease or IgE-mediated allergies to wheat often react to wheat, rye and barley. Protein inhibitors of proteases and α-amylases of cereals have also been described as both inhalant (e.g. Baker's asthma) and food allergens. A number of other proteins have been described as allergens in Baker's asthma and includes Tri a Bd 17K, a wheat peroxidase.	Seed storage prolamins α-amylase/ trypsin inhibitors Glycosylated peroxidase	Gliadins, glutenins (wheat gluten proteins) together with homologues from barley (hordeins) and rye (secalins) Members of the CM (chroloform-methanol) soluble proteins including CM3 Tri a Bd 17K
Fresh fruits and vegetables Kiwi	Fruit allergy is often associated with allergy to tree and grass pollen and to latex allergy. Thus, individuals who develop allergy to birch pollen tend to be allergic to a major birch pollen protein called Bet v 1. Related proteins are found in other plant species and edible tissues of fresh fruits and vegetables. Consequently when people	Homologues of the major birch pollen allergen Bet v 1 Cysteine	Act c 1 of kiwi fruit

Peach Celery	who have a Bet v 1-type birch pollen allergy eat fruits such as apples they often experience a reaction to the fruit which is confined to the oral cavity. The latter reaction has been termed oral allergy syndrome (OAS). Many *Rosaceae* fruits are involved in this pollen-fruit allergy syndrome, together with vegetables such as celery. In general these types of allergens are rapidly destroyed by cooking except for the form found in celery which can retain its allergenic activity even in soups. 00 Other types of fruit allergy occur where there is no association with a prior pollen or latex allergy, notably kiwi fruit allergy, which involves the cysteine proteinase actinidin. Similarly allergies to peach and related *Rosaceae* fruit found in southern Europe and can often be life-threatening being more akin to the peanut allergies experienced in the USA or UK. They are triggered by non-specific lipid transfer proteins which are thermostable and not destroyed by processing, the allergens even finding their way into fermented products such as wine and beer.	protease LTP	Pru p 3 of peach Api g 1 of celery,

REGULATION OF ALLERGENS IN FOODS

It has been estimated that around 95% of food allergic reactions are caused by several major groups of food allergens. However such estimates are imprecise, and debate about which allergens should be the subject of mandatory label warnings accounts for the fact that it took until 2003 (EU) and 2004 (USA) to determine regulatory lists.

The EU Commission Directorate General Health and Consumer Protection website describes the labelling regulations in Europe in full at
http://europa.eu.int/comm/food/food/labellingnutrition/index_en.htm

A Council Directive 2003/89/EC, amending the main Labelling Directive 2000/13/EC, abolishes the “25% rule” (former exemption of a compound ingredient, comprising less that 25% of the food, from declaration of its components) and requires manufacturers to declare any of a specified list of allergens present, or any product derived from such allergens (unless specifically exempted) (http://www.foodallergens.info/industry/fl_com2003-89_en.pdf)

In USA, regulation is by the Food Allergen Labeling and Consumer Protection Act of 2004
http://www.cfsan.fda.gov/~dms/alrgact.html

The English legislation giving effect to EU Directive 2003/89/EC is The Food Labelling (Amendment) (England) (No. 2) Regulations 2004
http://www.legislation.hmso.gov.uk/si/si2004/20042824.htm , which came into force on 26 November 2004. Similar Regulations apply respectively to Scotland, Wales and N Ireland. Further amendments have been introduced to this labelling framework and implemented in England through The Food Labelling (Amendment) (England) (No.2) (Amendment) Regulations 2005 SI 2005 No 2969; The Food Labelling (Declaration of Allergens) (England) Regulations 2007 SI 2007 No 3256 and The Food Labelling (Declaration of Allergens) (England) Regulations 2008 SI 2008 No 1188. Again, parallel legislation exists in Scotland, Wales and N Ireland. The English SIs are available, respectively, at:

http://www.opsi.gov.uk/si/si2005/uksi_20052969_en.pdf
http://www.opsi.gov.uk/si/si2007/pdf/uksi_20073256_en.pdf
http://www.opsi.gov.uk/si/si2008/pdf/uksi_20081188_en.pdf

The gluten proteins of wheat that trigger Coeliac disease can also cause IgE-mediated allergies. The inclusion of wheat in the WHO and EU allergen lists covers both its allergenic properties and its Coeliac toxic effects although the dose-response and management issues regarding these diseases are distinctly different.

Although the EU Directive allows for the maintenance of a limited number of derogations (exceptions) for the declaration of components of some categories of compound ingredients, it includes a list of ingredients or substances causing most cases of food allergies or intolerance (Table 2, below) – in this case no derogation (exception) is allowed unless the derivative has been fully evaluated by EFSA and subsequently specifically provided for in the legislation.

Table 2: Major Allergenic Foods Listed in Annex IIIa of the EU Directive on Labelling of Foods which must be declared

Cereals containing gluten, (i.e. wheat, rye, barley, oats, spelt or their hybridized strains) and products thereof
Crustaceans and products thereof
Eggs and products thereof
Fish and products thereof
Peanuts and products thereof
Soybeans and products thereof
Milk and products thereof (including lactose)
Nuts i.e. Almond, Hazelnut, Walnut, Cashew, Pecan nut, Brazil nut, Pistachio nut, Macadamia nut and Queensland nut and products thereof
Celery and products thereof
Mustard and products thereof
Sesame seeds and products thereof
Sulphur dioxide and sulphites at concentrations of more than 10mg/kg or 10 mg/liter expressed as SO_2.

As from 2007, molluscs and lupins, and products thereof, were added to the above list.
The derivatives for which exemptions are listed are those which are deemed no longer to retain the allergenic DNA (EU, 2005). Commission Directive 2007/68/EC bringing together the requirements from Directive 2003/89/EC, the amendment that added lupin and molluscs to the Annex IIIa list (Commission Directive No. 2006/142/EC) and the permanent exemptions for certain derived ingredients may be found at:
http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2007:310:0011:0014:EN:PDF
In order to implement these Regulations, manufacturers must have a detailed knowledge of the constituents of a product from each stage of the supply chain. This poses few problems for “simple” ingredients like wheat flour or milk powder, but becomes quite complex when compound foods are involved. Robust inventory and traceability systems need to be in place to manage the process, which include tracking changes in formulation of manufactured foods. Manufacturers often use different materials to achieve the same “functionality” in a particular product, depending on availability and cost. Such switching of materials is more difficult where an allergen declaration is required.

The Directive and the UK regulations do not specify the format in which Allergen declaration must appear other than that in general they must be included in (the usually small print of)

the list of ingredients. Since 1997 IFST has advocated that in addition, they should be more prominently drawn to attention of intended purchasers, for example by naming the allergen present in a separate box headed "Allergy Information" and some manufacturers and retailers are doing that. It is also important that they be named in a way that conveys their meaning to the public, for example "milk protein" rather than "casein" or "whey". Although this format of declaration is voluntary, in the UK if it is used it should name all the allergenic ingredients.

The UK Food Standards Agency has produced a detailed guidance document which can be found at http://www.food.gov.uk/multimedia/pdfs/allergenlabelguide08.pdf
.
In USA, regulation is by the Food Allergen Labeling and Consumer Protection Act of 2004 (FALCPA) (US FDA, 2004). All packaged foods regulated under the Act that are labelled on or after January 1 2006, must comply with its food allergen labeling requirements

FDA's list of allergens that must be indicated in labelling is

> Milk, egg, fish, crustacean shellfish, tree nuts, wheat, peanuts, soybeans (or protein derived from any of them).

FDA has produced an on-line Guidance for Industry: Questions and Answers Regarding Food Allergens, including the Food Allergen Labeling and Consumer Protection Act of 2004 (US FDA, 2006). In an FDA Guidance document on Frequently Asked Questions About Medical Foods, issued on 16 May 2007, it stated that the labelling requirements apply equally to medical foods (US FDA, 2005a)

Not to be outdone, on 7 July 2005, the US Department of Agriculture (USDA) Food Safety and Inspection Service issued a Notice to inspectors, giving instructions for verifying that establishments have the appropriate process controls in place for meat and poultry materials that can trigger food allergies and intolerances). The Notice was prompted by the number of recalls because of undeclared presence of ingredients that are capable of causing adverse reactions.

THE RESPONSIBILITIES OF INDIVIDUALS

No form of warning about the presence of an allergen in a food can be effective for an individual unless he or she is aware of the foods or food substances to which he/she is allergic. This information cannot be derived from any source except that individual and his/her medical adviser. People who think that they suffer from a food allergy owe it to themselves to undergo tests to determine if it is a true allergy, and if so, what is the substance that causes it. There are two methods of determining whether a person is allergic to a food or food substance. The first and simpler is the skin test. The second, more elaborate, but more definitive, is the double-blind, placebo-controlled oral challenge test.

CROSS-CONTACT ALLERGENS AND THE RESPONSIBILITY OF FOOD MANUFACTURERS

The EU Directive does not address the problems of allergens that enter foods accidentally. These are sometimes referred to as "cross-contact" allergens. The adventitious presence of an allergen in a product may arise in three main ways

- cross-contact of an ingredient before or after it is received;
- accidental mis-formulation;
- cross-contact by an allergen from a different product.

Cross-contact of an ingredient or a product by an allergen from a different ingredient or product may arise in storage and handling of raw materials, or during production due to residues in shared equipment, airborne dust, or the improper incorporation of re-work material without consideration of the allergen problem.

Mis-formulation resulting in the inclusion of an allergen (or any other ingredient) not in the product formulation recipe should be prevented by proper attention to the formulation development and the operation of appropriate control provisions to ensure that the product as prepared contains only the ingredients specified.

It should be emphasised that the importance of prevention of cross-contact applies not only to a product nominally free from allergens, but equally to a product containing one or more declared allergens at risk of cross-contact by others

In order to develop the most cost-effective systems for managing food allergens a knowledge of how much of an allergenic food is needed to trigger an adverse reaction in the body, which allergen(s) in the food must be monitored, and how the allergen behaves during processing, is needed. Unfortunately, knowledge regarding these factors is lacking and research is still needed in order to set limits for levels of allergens in foods in relation to their labelling. Thus, the threshold doses that elicit allergic reactions, and the establishment of appropriate reference analytical methodology for detection of traces of allergens remain to be defined.

Nevertheless food manufacturers have a responsibility to minimise the risks to allergen-susceptible consumers of their products. As with any other food-related hazards, action should be based on carrying out a HACCP-style analysis of the operations in relation to allergen hazards. This should lead to adoption of appropriate measures. In a multi-product company, the ideal would be complete segregation in different buildings, which some companies have done. In any event appropriate measures should include:

- to formulate foods so as to avoid, wherever possible, inclusion of unnecessary major allergens as ingredients;
- to organise raw material supplies, storage and handling, production procedures, production schedules and cleaning procedures so as to prevent cross-contact of products by "foreign" allergens;
- to train all personnel in an understanding of necessary measures and the reasons for them;
- to comply with the relevant labelling legislation providing appropriate warning, to potential purchasers, of the presence of a major allergen in a product;
- to have in place an appropriate system for recall of any product found to contain a major allergen not indicated on the label warning.

PRECAUTIONARY LABELLING

In response to the problems posed by cross-contact allergens and the lack of resources to implement appropriate control systems (which ideally could mean building dedicated allergen-free factories) many manufacturers have adopted a “precautionary labelling”

approach. Precautionary statements such as 'may contain' are expressly allowed in Australia and New Zealand and are used widely in these countries. In the UK, longstanding industry guidelines state clearly: "It is emphasised that the use of advisory, "may contain" labelling should be the last resort of a series of assessments. It should never be used as an alternative to GMP and relevant controls." However, unless responsibly applied by the manufacturer as a last resort following a thorough assessment of each product on a case-by-case basis, such labels do not help allergic consumers cope with their condition and may mean their food choices become ever more restricted. Such labels, if applied without the necessary risk assessment, can be viewed also as a cover for sub-optimal allergen control practices, and may run the risk of devaluing the label itself, as indicated in a small qualitative study undertaken by the UK Food Standards Agency (http://www.food.gov.uk/multimedia/pdfs/nutallergyresearch.pdf).

There is anecdotal evidence that some allergic consumers (regularly) ignore precautionary labels, putting themselves at a potential risk, and for these individuals provision of more meaningful information about cross-contact allergens may enable them to make their own choices. Other types of allergic consumer prefer the manufacturers to take responsibility for deciding which products are suitable for someone with an allergy with clear negative (e.g. "not suitable for nut allergy sufferers") or positive (e.g. "This product is nut-free") statements, though it is not clear how "not suitable for …" provides greater consumer choice than "may contain". There are issues regarding provision of more information on allergens on crowded food labels and conflicts with the need to make them clear and simple to read.

Allergic consumer groups, such as the European Federation of Allergy and Airways Diseases Patients' Associations (EFA) are beginning to call for the EU to regulate precautionary labelling. It may also be useful to back-up information on labels with additional background information to facilitate interpretation of labels. However, the preferences of different end-users regarding the format that such information should take, and the type of additional information required to back-up what is provided on the label still need to be defined.

FOODSERVICE RESPONSIBILITIES AND PROBLEMS

Reference has already been made to the responsibility of individuals with an allergy to find out to what substance(s) they are allergic. Only then can they make use of warning information. This also applies when eating food prepared by others.

In this context foodservice may be viewed as a particular kind of manufacture with added complications. In general, the principles referred to for product formulation and avoidance of cross-contact by manufacturers apply equally to foodservice providers; and similar warnings should be given adjacent to appropriate items on menus or self-service display notices.

In some large restaurant chains, the expertise exist to do this, and their buying power enables them to lay down specifications and monitor performance of ingredient suppliers; but many small foodservice outlets have neither that expertise nor buying power. Label warnings on bulk packs supplied by manufacturers for foodservice use may be of some help but such information must remain readily available after the packs have been opened.

An additional problem arises, however, in an establishment where a chef has a free hand in creating dishes. It is important, therefore, that chefs are given training in recognition of the major allergens, the principles of minimising risk in respect of them and the need to notify any use of allergens, including their use in ways that might go unnoticed by others, for example use of an egg glaze on pastry.

Food Allergy

Throughout foodservice, the main cross-contact problem is that due to common use of equipment such as ladles, which inevitably happens in busy kitchens despite admonitions to the contrary.

In parts of the foodservice field, such as aircraft in-flight meals in economy (coach) class (where there is normally neither printed menu nor display) the problem of giving adequate warnings is far more difficult to solve. The same applies to the multiplicity of small foodservice outlets, where, in addition, many proprietors would not have sufficient knowledge to know what warnings to give.

With in-flight meals, the problem is compounded by having to deal with a tray containing several components (starter, main course, dessert, roll/bun and butter, cheese). Moreover, it is not like a situation where someone who is, for example, allergic to soya can look at the label of a food product before purchase, find a soya warning and decide not to purchase.

Aircraft meals are prepared in so-called "central kitchens" which are really factories manufacturing short-life high risk ready meals under stringent conditions of hygiene, and have technical managers with the expertise to deal with the minimisation of unnecessary allergens in recipes, monitoring of their suppliers, prevention of cross-contact and provision of warning information. One solution would be for the central kitchen to provide a menu (which could be just a sheet of paper), with each item carrying a warning of any major allergens present, and cabin staff distributing this to passengers in advance of meal selection. Another solution could depend on cabin staff being provided with such an annotated menu list and passengers being asked on the address system "If you have a food allergy, please tell the cabin staff what you are allergic to and they will be able tell you if that is present in any part of the meals available".

The situation is very different in small foodservice outlets (or in many larger restaurants), and street vendors. For the allergy sufferer to say "I am allergic to X. Is there any X in dish Y?" may or may not produce an accurate answer where the allergen is very obvious as a direct component of the dish, but is most unlikely to do so where X is a sub-component in, say, a sauce or a soup. Furthermore the question may well be put to a transient low-paid employee whose first language may, in addition, not be the language in which the question is put.

Foods sold loose, or from foodservice outlets represent a considerable risk to allergic consumers. The UK Food Standards Agency has developed some guidance for the catering (foodservice) industry (UK FSA, 2005). In USA, the Hospitality Institute of Technology and Management has produced guidance for caterers and retailers (Snyder OP, 2005).

The UK Food Standards Agency has also produced a best practice guide in January 2008 on the provision of allergen information for foods sold non-prepacked - this covers foods sold loose, as well as those packaged at the point of sale and also catering.
http://www.food.gov.uk/foodindustry/guidancenotes/labelregsguidance/nonprepacked

MEASURING ALLERGENS IN FOODS

In the wake of Directive 2003/89/EC and the problems posed by cross-contact allergens in foods. there is a need to be able to detect allergens in foods both for the food industry in setting up and maintaining allergen hazard control procedures, and for those involved in enforcing the legislation. In this respect, it must be noted that the laws requiring labelling of the designated allergens do not provide for any thresholds below which the presence of the

allergen or its derivatives may be discounted, except in the case of sulphite and the limited list of derivatives that have been assessed by EFSA as no longer possessing allergenic potential.

How much allergen does it take to cause a problem?

In order to control allergens in foods effectively, it is important to know how much of an allergen (or allergen containing food) can trigger an allergic reaction in an individual. A threshold dose is defined as the lowest observed adverse effect level (LOAEL), an amount of a specific food that would elicit mild, objective symptoms in highly sensitive individuals. Double-blind, placebo-controlled food challenges (DBPCFCs) conducted in panels of food allergy sufferers with low doses of specific allergenic foods demonstrate rather clearly that finite threshold doses exist below which allergic consumers will not react. Individuals with IgE-mediated food allergies appear to vary rather widely in their degree of sensitivity to specific allergenic foods. For example, in DBPCFCs with peanut-allergic individuals, individuals threshold doses ranged from 2 mg to >50 mg, as defined on the basis of objective symptoms. Threshold doses for peanut, egg, and cows' milk appear to be in the low milligram range or higher for individuals with allergies to those specific foods.

However, these data are often obtained using different protocols making the estimation of a threshold dose rather difficult. In particular there is a need for no observed adverse effect level (NOEL) data which is currently lacking and has led to the observation by both the EFSA Panel on Dietetic products, Nutrition and Allergies (http://www.efsa.eu.int/science/nda/nda_opinions/341/opinion_nda_04_en1.pdf) and more recently the US FDA Threshold working group's draft report (http://www.cfsan.fda.gov/~Dms/Alrgn.Html) that current clinical data are insufficient. In particular more data are needed on low-dose challenges of individuals with specific food allergies to establish NOEL's using a consistently applied clinical protocol to obtain better estimates of threshold doses for various foods. This is one of the goals of the Food Allergy Research and Resource Programme (FARRP; http://www.farrp.org/), based in the USA but working internationally with clinicians and the food industry to establish objective information on thresholds for all the major allergenic foods that will have to be labelled. More information will also come from EU funded research (http://www5.ifr.bbsrc.ac.uk/europrevall/) which will complement that being produced by FARRP.

While low doses of allergenic foods clearly can present some risk to allergic consumers, the imposition of a zero tolerance level for undeclared allergens in such foods places unachievable burdens on the food industry. Some food companies manufacture many different food products within the same processing facility and many different products can be manufactured within a single building. In such situations, unless segregation of materials and production lines is practised, trace residues of a specific food could come into contact with another food being manufactured in the same facility. Furthermore, the food industry often uses shared equipment to manufacture related food products, e.g. ice cream and sorbet or chocolate confections with differing ingredients. Reliable information on threshold doses would valuably contribute to ability to monitor cross-contact allergens through, for example, clean-down procedures for common processing equipment and thereby the implementation of prudent sanitation practices for shared equipment or facilities.

What to analyse for?

Almost all allergens are proteinaceous in nature and highly sensitive analytical methods have been developed using either immunoassays or PCR-based methods to detect traces of allergenic foods resulting from such common industry practices. A number of methods have

been developed for analysis of many major allergenic foods listed in Annex IIIa of the draft labelling directive, some of which are commercially available in kit-form.

The detection and especially the quantification of allergens in processed food products can be very difficult, as they are often present in trace amounts only, or are masked by the food matrix. For example, peanuts available in the food sector are derived from various sources, and are processed in various ways, such as dry and oil roasting. This can lead to a significant variation of the protein content and profile, and the detectability in different batches of peanuts.

As well as dealing with the problems of the food matrix, methods must also be sensitive enough specifically to detect the allergens in those amounts that might trigger allergic reactions in sensitised individuals. There are anecdotal accounts of serious peanut allergies, for example by parents about their children and about airline travellers affected by someone a few rows away eating peanuts. However it has been shown that a level of 100 micrograms of peanut proteins can trigger a mild reaction in a peanut allergic person (such as tingling in the mouth or itching), although the threshold where objective symptoms (such as skin rashes, inflammation and swelling, asthma, anaphylaxis) for peanut is much higher (in the low milligram range). Although there is some debate in the scientific community about the relative importance of subjective and objective symptoms in terms of determining thresholds, there is a general consensus that they should be based on objective symptoms as these are a more reliable indicator if clinical reactivity.

100 micrograms could result from the consumption of a 100 g chocolate bar containing 1 mg/kg peanuts. In order to detect this amount of peanut the limits of detection on an assay would to be in the range of 1 to 100 mg/kg. In order to standardise analytical methodology available the European Committee for Standardisation (CEN) has recently established a new working group on food allergens (CEN TC 275 WG 12). There are wide variations in commercial kit performance and the CEN working group concluded that there were no collaboratively trial tested (validated) methods available so far for the analysis of allergens in low ppm ranges. Reference materials for allergens are also required in order to validate and calibrate analytical methodology yet none are currently avaIable. A peanut reference material based on commonly used peanut varieties both for research and routine analysis is currently being produced by the EC's Joint Research Centre. This peanut reference standard will also take into account specific demands from the food industry and respect various nut roasting conditions.

ALLERGENIC POTENTIAL OF GM FOODS AND NOVEL FOODS

In many countries an assessment of the allergenic risks posed by a GM food or a novel food must be performed before it can be released into the market. The European Union defines a novel food as any food which has not previously been used for human consumption to a significant degree within the Union before May 1997. Separate legislation applies to products developed with the aid of genetic modification, but the general principles (if not the precise, scientific detail) of pre-market assessments of allergenic potential are similar.

Unlike many aspects of chemical toxicity, the allergenicity of a protein is not completely predictable. Our understanding of the molecular mechanisms underlying the development of aberrant IgE responses of allergy is at present incomplete and as a result any risk assessment regarding allergenicity has to rely on a cumulative body of evidence of many different types. Factors that are important include the genetic factors relating to the susceptibility of an individual to becoming allergic (What makes an individual allergic?), the structural features of allergens that predispose them to triggering allergic responses in

susceptible individuals (What makes a protein an allergen?) and environmental factors may attenuate the dialogue between an individuals digestive and metabolic processes and an allergen. For example, it is thought that infections in childhood may play an important role in reprogramming the immune system so that it becomes less prone to allergies. The food matrix may also affect the presentation of allergens to the immune system, altering allergic responses. Food consumption habits may affect the patterns of allergies to different foods in different countries and allergies to certain fruits and vegetables are associated with prior allergy to birch pollen and hence are related to the geographic distribution of birch trees

Assessing the allergenic activity of a GM food or a novel protein

As a consequence of this complexity, and the deficiencies in our current understanding of the causes of food allergy and lack of good model systems, any allergenic risk assessment process must rely on information from a number of different sources. It also needs to take account of the ability of an allergen to act in both the sensitisation and elicitation phases of an allergic response.

Decision-tree approaches have been proposed to facilitate this assessment, initially by the International Life Science Institute (ILSI) in conjunction with the Food Biotechnology Council in 1996 (Metcalfe et al 1996), with a revised version proposed by a joint FAO/WHO Expert Consultation on Foods Derived from Biotechnology (WHO-FAO, 2001).

However, the third session of the FAO-WHO Codex Alimentarius Commission Ad Hoc Intergovernmental task force on Foods Derived from Biotechnology (ALINORM 03/34) decided in March 2002 not to elaborate the decision tree approach. As no single criterion is sufficiently predictive of allergenicity, they recommended that the risk assessment process should adopt an integrated step-wise case-by-case approach which takes account of information of several types. Such an integrative approach would be likely to include information on

- relationships between novel proteins and known allergens, defined using bioinformatics tools,
- cross-reactivity defined using patient allergic sera,
- *in vitro* measures of protein digestibility
- *in vivo* sensitisation using animal models.

Bioinformatics: There are now hundreds of food and respiratory protein allergens which have been sequenced and characterized. This resource can be used to address questions regarding novel proteins as to whether it is a known allergen and whether it is likely to cross-react with a known allergen. However, such bioinformatics approaches are NOT intend to answer whether a protein will “become” an allergen or not.

Human allergic sera: In general allergens can most easily defined using methods based on their ability to elicit reactions in already sensitised individuals (either humans or laboratory animals). These methods include

- *In vitro* serological tests such as immunoblotting and immunoassay which all use sera from individuals with a known allergy which contain IgE which binds to the allergens
- *In vitro* cellular tests which measure the ability of allergens to degranulate basophils/mast cells from individuals with a known allergy (or cell-lines which can be sensitised with serum IgE from allergic individuals) and to provoke the release of pharmacologically active mediators

- *In vivo* skin prick tests where a tiny (ng-μg) quantity of allergen is introduced into the skin of an allergic individual and any resulting skin rash assessed.
- *In vivo* oral administration of allergens where individuals are given doses of allergens (or the foods they come from) to eat (sometimes disguised in another food) and monitored for symptoms associated with allergic reactions.

Of these methods the first two are the ones most widely used. *In vivo* testing in humans is much more complex and requires ethical approval before it can be undertaken.

In vitro digestion: One of the major biological processes that food undergoes before it comes into contact with the immune systems is digestion. As peptides require a molecular weight of greater than 3,000 Daltons in order to stimulate an immune response, large stable fragments, as well as intact proteins, have the potential to act as sensitizers. Consequently resistance to pepsin digestion has become enshrined in the approaches used for assessing the allergenic potential of novel proteins. However, there is much debate as to its validity as the apparent stability of a protein can be very dependent on the experimental conditions employed. The pepsin digestion protocols that have been employed typically involve substrate:pepsin ratios in the range 5:1 – 10:1. Such ratios may be considered far in excess of those likely to be found in the stomach and it can be estimated that a typical adult dietary intake of protein around 75g/24h would give a ratio of ~ 3mg protein/unit pepsin secreted compared to ~ 4μg protein/unit pepsin used during digestion assays.

Animal models of sensitisation: Unfortunately at present there are no agreed methods for assessing the ability of proteins to act in the first phase of allergy – i.e. sensitisation. It has become increasingly evident that small mammals, such as mice and rats, do not mimic the ability of humans to become sensitised via the oral route. Such sensitisation of small mammals requires the addition of substances known as adjuvants, such as cholera toxin or polysaccharides such as carrageenan, before sensitisation occurs.

Conclusions

The evidence to date supports the view that the allergenic risks posed by GM foods, are generally no greater than those posed by new crops and foods developed by traditional methods. The allergenic risk assessment process currently employed to determine the safety of candidate transgenes makes it highly unlikely that a ‘novel’ food allergen would be introduced into the market. The methods referred to above may be used for novel foods but because one may be dealing with protein(s) not previously encountered, the situation is potentially more problematic. However, it is clear that such an assessment process will be more effective once our understanding of the molecular basis of allergenicity has improved. Information resulting from research into what makes an individual become allergic and what makes some proteins, and not others, become allergens, will undoubtedly underpin the development of integrative methods for more effective assessment of the allergenic potential of novel foods.

There is, however, a possibility that genetic modification could be used in future to modify allergenic foods to render them hypoallergenic, for example by "switching off" or blocking the reaction by which the immune system recognises the allergenic substance as an invader and reacts by generating the antibodies that cause the release of histamines. Beginning as an effort to understand the risks of potential allergens in GM foods, research is proceeding at Tulane University, New Orleans, to develop hypoallergenic prawns, while similar research is proceeding at University of Arkansas to develop hypoallergenic peanuts.

FOOD ALLERGY RESEARCH

This should aim to increase our understanding of the molecular basis of allergic disease has improved. Information resulting from research into what makes an individual become allergic and what makes some proteins, and not others, become allergens, will provide even more effective assessment of the allergenic potential of novel foods. While there are plenty of anecdotal accounts, particular regarding peanut, where extremely small amounts have caused serious reactions, the most difficult research area, and one with ethical considerations, is that of determining threshold levels of different allergens causing allergic reactions in individuals very sensitive to those allergens (US FDA 2005).

The UK Food Standards Agency has a significant food allergy and food intolerance research programme to improve the understanding of the causes and mechanisms of food allergy. www.food.gov.uk/science/research/researchinfo/foodcomponentsresearch/allergyresearch

EuroPrevall is an EU-funded multidisciplinary integrated project (IP) involving 16 European member-states, Bulgaria (a candidate country), Switzerland and Iceland, plus Ghana and now New Zealand and Australia. Of the 55 partners, there are 15 clinical organisations, three major manufacturers and six small-medium sized enterprises (SMEs) as well as the leading allergy research organisations in Europe.

EuroPREVALL research will:

- Characterise the patterns and prevalence of food allergies across Europe in infants, children and adults
- Develop methods to improve the quality of food allergy diagnosis, reducing the need for food challenge tests
- Determine the impact of food allergies on the quality of life and its economic cost for food allergic people and their families, workplace and employers, and healthcare.

A new line of research which might reap huge benefits some years down the line, stems from the discovery that nanoparticles of 60-carbon-atom buckminster-fullerenes, so-called “bucky balls”, which are powerful antioxidants, when incubated with human cell cultures and subjected to an immune system challenge, resulted in a significant reduction of mast cell histamine formation and inhibition of inflammation. The human cell cultures grow normally in the presence of these nanoparticles. Trials in mice showed significant reduction in anaphylaxis (Kepley C, 2007).

Key references

Asero R et al (2007). IgE-Mediated food allergy diagnosis: Current status and new perspectives. *Mol Nutr Food Res* 2007, **51**, 135-147.

Anaphylaxis Searchable Database. http://www.anaphylaxis.org.uk/db/TACstart.php

Buchanan A et al (2007). Egg oral immunotherapy in nonanaphylactic children with egg allergy. *J. Allergy Clin. Immunol.*, on-line ahead of print. doi: 10.1016/j.jaci.2006.09.016 http://www.aaaai.org/media/jaci/2007/02/buchanan.stm

Bush RK, Hefle SL. Food allergens. Crit Rev Food Sci Nutr. 1996;36 Suppl:S119-63. (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=8959381)

Clark AT et al (2009), *Allergy* "Successful oral tolerance induction in severe peanut allergy". Published online ahead of print, doi: 10.1111/j.1398-9995.2009.01982.x
http://www.wellcome.ac.uk/index.htm

Codex General Standard for the Labelling of Prepackaged Foods (1999) CODEX STAN 1-1985 (Rev. 1-1991).
(http://www.fao.org/DOCREP/005/Y2770E/y2770e02.htm#bm02)

EUROPEAN UNION. Directive 2000/13/EC of the European Parliament and of the Council of 20 March 2000 on the approximation of the laws of the Member States relating to the labelling, presentation and advertising of foodstuffs. *Official Journal* L **109**: 6.5.2000, P. P0029-0042.
http://europa.eu.int/comm/food/food/labellingnutrition/foodlabelling/comm_legisl_en.htm

EUROPEAN UNION. Directive 2003/89/EC of 10 November 2003 amending Directive 2000/13/EC as regards indication of the ingredients present in foodstuffs
Official Journal L
http://www.foodallergens.info/industry/fl_com2003-89_en.pdf

EUROPEAN UNION. Directive 2005/26/EC of 21st March 2005 esablishing a list of food ingredients or substances provisionally excluded from Annexx IIIa of the Directive 2000/13/EC of the European Parliament and of the Council *Official Journal* L **75:** 22.3.2005, P0033-0034.(http://europa.eu.int/eur-lex/lex/LexUriServ/site/en/oj/2005/l_075/l_07520050322en00330034.pdf)

EUROPEAN UNION. (2004) Opinion of the Scientific Panel on Dietetic Products, Nutrition and Allergies: Evaluation of allergenic foods for labelling purposes
The EFSA Journal 32: 1-197.
http://www.efsa.eu.int/science/nda/nda_opinions/341/opinion_nda_04_en1.pdf

FAO-WHO Ad Hoc Intergovernmental task force on Foods Derived from Biotechnology (ALINORM 03/34)
(http://www.codexalimentarius.net/web/archives.jsp?year=03)

FAO-WHO Expert Consultation on Foods Derived from Biotechnology (2001).
(http://www.who.int/foodsafety/publications/biotech/en/ec_sept2001.pdf)

Herian AM et al (1990). Identification of soybean allergens by immunoblotting in sera from soy-allergic adults. *Int. Arch. Allergy Appl. Immunol*., **92**, 193-198.

Hileman RE et al (2002). Bioinformatic methods for allergenicity assessment using a comprehensive allergen database. *Int Arch Allergy Immunol*. 2002;128(4):280-91. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12218366

Hourihane JO et al (1997). Randomised, double blind, crossover challenge study of allergenicity of peanut oils in subjects allergic to peanuts. *British Medical Journal*, 314, 12 April 1997, 1084-8.

Kepley C (2007). Researchers Develop Buckyballs to Fight Allergy.

http://www.news.vcu.edu/news.aspx?v=detail&nid=2121

Metcalfe DD, Astwood JD, Townsend R, Sampson HA, Taylor SL, Fuchs RL. Assessment of the allergenic potential of foods derived from genetically engineered crop plants. Crit Rev *Food Sci Nutr*. 1996;36 Suppl:S165-86.

Mills ENC et al (2004). Information provision for allergic consumers – where are we going with food allergen labelling? *Allergy*, December 2004, vol. 59(12) pp. 1262-1268. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=15507093

Olszewski et al, "Isolation and characterization of proteic allergens in refined peanut oil" .*Clin Exp Allergy* (1998);**28**(7):850-9

Nørhede P (2007). Food allergy diagnosis today and in the future. http://admin.ga2len.net/files_new/filesPublic/Educ_FoodAllDiagnosis_paper_Final.pdf

Sampson HA. Update on food allergy. *J Allergy Clin Immunol*. 2004 May;113(5):805-19 (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=15131561)

Snyder, OP, Hospitality Institute of Technology and Management, "Management of Adverse Food Reactions in Retail Food Operations" at http://www.hi-tm.com/Documents2005/allergens-retail-and-list.pdf

UK Committee on Toxicity (2008). Statement on the Review of the 1998 COT Recommendations on Peanut Avoidance. http://cot.food.gov.uk/pdfs/cotstatement200807peanut.pdf

UK Food Standards Agency (2005). Advice for caterers on allergy and intolerance. http://www.food.gov.uk/safereating/allergyintol/caterers/

UK Food Standards Agency (2008). Guidance on food allergen labelling legislation http://www.food.gov.uk/multimedia/pdfs/allergenlabelguide08.pdf

UK Food Standards Agency. Providing allergen information for non pre-packed foods. http://www.food.gov.uk/foodindustry/guidancenotes/labelregsguidance/nonprepacked

UK Food Standards Agency (2008). Food Intolerance including Food Allergy Research Programme(T07) www.food.gov.uk/science/research/researchinfo/foodcomponentsresearch/allergyresearch

USDA FSIS (2005) Notice "*Verification of Activities Related to an Establishment's Controls for the Use of Ingredients of Public Health Concern*". http://www.fsis.usda.gov/regulations_&_policies/Notice_45-05/index.asp

US FDA Threshold Working Group (2005) Approaches to Establish Thresholds for Major Food Allergens and for Gluten in Food DRAFT REPORT http://www.cfsan.fda.gov/~Dms/Alrgn.Html

US FDA (2006) Questions and Answers Regarding Food Allergens, including the Food Allergen Labeling and Consumer Protection Act of 2004' http://www.cfsan.fda.gov/~dms/alrguid.html

US FDA (2007) Frequently Asked Questions About Medical Foods.

http://www.cfsan.fda.gov/~dms/medfguid.html

Wal JM, Pascal G. Benefits and limits of different approaches for assessing the allergenic potential of novel foods. *Allergy*. 1998; 53(46 Suppl):98-101.

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Competence, integrity, and serving the public benefit lie at the heart of IFST philosophy. At all times IFST aims to:

- Benefit the public supply of safe, wholesome, nutritious, tasty and attractive food through the application of sound science and technology;
- Improve public knowledge and awareness of important issues relating to the supply, production, safety and quality of food;
- Develop and communicate the knowledge underlying food science and technology, and further the education of food scientists and technologists;
- Safeguard the public by defining, promoting, and upholding professional standards of competence, integrity and ethical behaviour; and
- Maintain these standards by encouraging members to continue their professional education and development throughout their careers.

In serving the public benefit IFST takes into account the many elements that are important for the efficient and responsible supply, manufacture and distribution of safe, wholesome, nutritious, and affordable foods with due regard for the environment, animal welfare and the rights of consumers.