

FOOD STANDARDS AUSTRALIA NEW ZEALAND

Review of the regulatory management of food allergens

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Executive Summary

Food allergy is an important health issue due to the potential for severe and life threatening reactions. Rigorous declaration requirements are considered the most appropriate risk management option for food allergens since even small amounts of the allergen may trigger allergic reactions. Australia and New Zealand were among the first countries to recognise the need to regulate food allergens with the introduction, in 2002, of mandatory declaration requirements in the Australia and New Zealand Food Standards Code.

In October 2006, the Australia and New Zealand Food Regulation Ministerial Council requested FSANZ to review the regulatory management of food allergens. The overall aim of the review is to determine whether, in the context of current scientific knowledge, improvements can be made to the existing regulatory approach which allows consumer choice but does not compromise the safety of allergic consumers.

A key task for the review was to identify specific areas of allergen regulation that could benefit from emerging scientific evidence. Six issues were outlined in a consultation paper, released by FSANZ in March 2008, targeting major stakeholders in Australia and New Zealand including allergy support groups, the food industry, allergy clinicians and the jurisdictions.

In reviewing these issues, FSANZ considered information from a variety of sources including allergic consumers, the food industry, the scientific and medical literature and expert opinion, as well as international regulations. Although our understanding of food allergy has improved significantly in the past decade, a number of scientific questions are yet to be resolved. The review identified information gaps which need to be addressed in order to strengthen the evidence base.

The review also provided an opportunity to consider the current requirements in light of industry initiatives to improve allergen control practices in the food production and processing environment.

This report presents the findings and conclusions of the review, and makes recommendations. One key recommendation, which has already been implemented by FSANZ, is the establishment of a Scientific Advisory Group to facilitate the integration of emerging clinical evidence into regulatory and non-regulatory approaches to food allergens.

A summary of the review findings and recommendations is presented below:

Issues	Main conclusions	Recommendations
1. New food allergens	<p>New food allergens may emerge that need to be considered for inclusion in the list for mandatory declaration. While the lists of food allergens may vary between countries, there is a need for an internationally consistent approach.</p>	<p>In consultation with the Food Allergy and Intolerance Scientific Advisory Group, FSANZ to develop a Proposal to amend Standard 1.2.3 to include lupin in the list of allergenic substances.</p>
2. Label information	<p>The use of clear terminology and easily understood names for ingredients present in food assists allergic consumers in recognising products they need to avoid. In general, regulatory requirements and additional voluntary declarations provide adequate information to allergic consumers to assist them in identifying ingredients of concern.</p>	<p>FSANZ to continue working with industry to support a voluntary system to improve allergen declaration generally, and to minimise the use of precautionary labelling through management of allergen cross contact.</p>
	<p>Precautionary labelling is recognised internationally as a difficult area to regulate. The science needed to answer relevant questions and to underpin decisions, such as allergen thresholds and the reliability of detection methods, is not available or is incomplete. Research is continuing to improve the evidence base and to establish robust risk assessment methodologies in this area.</p>	<p>In collaboration with the food industry, FSANZ to put in place a label monitoring program specifically designed to track improvements in allergen labelling practices with a particular focus on 'source' and precautionary labelling. The data gained would allow FSANZ to track the effectiveness of voluntary practices and would assist the industry in achieving its goal to provide accurate and useful information to allergic consumers.</p>
3. Food exempt from bearing a label	<p>Many of the allergic reactions that occur in the population are attributed to unlabelled food eaten outside the home, such as in restaurants and cafes.</p>	<p>With respect to allergen declarations in the food service sector, it is recommended that the Implementation Sub-Committee is asked to consider the communication of regulatory obligations to food businesses and to provide access to educational initiatives, with FSANZ's assistance as required.</p>
	<p>There are several groups involved in providing resources or implementing new initiatives to enhance the knowledge of the staff in the food service sector in relation to allergens. Overall there is an indication of the need for more effective means of communicating regulatory obligations.</p>	

Issues	Main conclusions	Recommendations
	<p>There is also a need to establish further education and training for staff at all levels in this sector.</p> <p>It is FSANZ's view that the current regulatory measures are adequate to manage the food allergy risks from foods exempt from bearing a label.</p> <p>However, there is a need for establishing more effective means of communicating these regulatory obligations and implementing initiatives to enhance the allergen management knowledge of workers in the food service sector.</p>	
<p>4. Labelling requirements for the current list of allergenic foods</p>	<p>Tree nuts: In line with the European and Canadian approach, a list identifying those tree nuts that are most relevant to food allergy in Australia and New Zealand will improve the clarity of the mandatory requirements.</p> <p>Fish: Molluscs and crustaceans are allergenically distinct from finfish. Therefore, the terms 'fish' and 'seafood' as defined in the Code, are not useful in the context of allergy to finfish, crustaceans and molluscs. Terms that allow consumers to identify the specific group would be more compatible with the intent and purpose of allergen declaration requirements.</p> <p>Cereals containing gluten: Gluten triggers coeliac disease and also appears to be a major source of allergens in wheat food allergy. It is now widely accepted that small amounts of gluten (around a daily intake of 10–20 mg) are tolerated by the majority of coeliac patients. It has also been suggested that most wheat allergic individuals can tolerate similar amounts of wheat protein.</p>	<p>FSANZ to consult with the Food Allergy and Intolerance Scientific Advisory Group on the development of a list of the tree nuts that are considered important allergens.</p> <p>FSANZ to consider this issue further in consultation with the relevant stakeholders in Australia and New Zealand. In particular, information from the food industry and food service sector in relation to current practices and commonly used terms, would assist in developing options to improve the clarity of the mandatory declaration requirements.</p> <p>FSANZ to consult with the Food Allergy and Intolerance Scientific Advisory Group on the current state of knowledge in relation to the wheat allergy, including cross-reactivity with other cereals, and if necessary, develop options to improve the clarity of the declaration requirements in relation to coeliac and wheat allergic patients.</p>

Issues	Main conclusions	Recommendations
<p>5. Exemption of ingredients derived from allergenic foods</p>	<p>Food processing can alter the allergenicity of food. Processes that physically or chemically separate food constituents can result in undetectable, or only residual, levels of protein in the processed products. However, reliable and easy to use protein detection methodologies are generally required to ensure process specifications are consistently achieved. Consideration of clinically relevant data is also required to determine the safety of food products derived from allergenic sources.</p>	<p>FSANZ to consider, on a case-by-case basis, the scientific and clinical data available on the allergenicity of food ingredients derived from allergenic sources. In consultation with the food industry, FSANZ to develop options to reflect the evidence base through guidance and/or regulatory amendments.</p>
<p>6. Allergen thresholds (level that triggers an allergic reaction)</p>	<p>Significant advances have been made in the area of thresholds in the last decade including improved methodologies for gathering and analysing clinical data. Emerging evidence indicates that statistical modelling approaches can be used to establish population threshold levels to underpin allergen risk assessment and guide allergen control measures in food manufacturing.</p>	<p>In collaboration with the Food Allergy and Intolerance Scientific Advisory Group, FSANZ to maintain a watching brief on scientific developments in the area of allergen thresholds.</p>

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1 Introduction

1.1 Background to the review

In October 2006, the Australia and New Zealand Food Regulation Ministerial Council requested that FSANZ conduct a review of the regulatory management of allergens. If necessary, FSANZ is to recommend a revised regulatory approach based on current scientific evidence which allows consumer choice but does not compromise the safety of allergic consumers.

1.1.1 Scope of the review

The scope of the review was guided by a number of issues that have arisen since the allergen regulations were developed a decade ago. As a first step in the review process, FSANZ released an Issues Paper for stakeholder consultation in March 2008, and held a number of teleconferences with interested stakeholders to facilitate input. Issues identified for review were:

1. New food allergens
2. Labelling requirements for the current list of allergenic foods
3. Label information
4. Allergenic thresholds (level that triggers an allergic reaction)
5. Exemption of ingredients derived from allergenic foods
6. Food exempt from bearing a label

The consultation specifically targeted stakeholder groups with significant interest in food allergens including the food industry, allergic consumers and their carers and allergy specialists in Australia and New Zealand. Australian and New Zealand regulatory partners were also invited to participate in this consultation. Stakeholder submissions received by FSANZ were taken into account in the development of the scope and direction of the review. FSANZ also undertook a number of projects to gather and generate data to inform the review.

The review was established to address the question of whether the regulatory management of food allergens is meeting the needs of allergic consumers in Australia and New Zealand. The aim is to determine whether, in the context of current knowledge, improvements can be made to the existing regulatory approach which allows consumer choice but does not compromise the safety of allergic consumers.

1.1.2 Process of the review

An important aspect of the review was to assess information from a wide range of sources to ensure emerging evidence and improvements in our understanding of stakeholder issues are reflected in our regulatory and non-regulatory approaches to food allergens. This required FSANZ to undertake a number of information gathering activities including consumer surveys, label monitoring surveys (including labelling surveys conducted by the industry) and scientific research. Developments in international regulations in this area were also considered by FSANZ to benchmark the regulatory approach in Australia and New Zealand to that of other major international regulations.

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Based on the information available, FSANZ explored the use of regulatory and non-regulatory options to address the issues of concern to stakeholders. The regulatory pathway includes identifying applications and/or proposals that could address these issues.

The non-regulatory pathway would include mechanisms for the consistent application of guidelines, procedures and risk management tools across various sectors of the food industry to achieve the desired outcomes. Any applications and proposals will be progressed according to the normal FSANZ process.

1.2 Food allergy

1.2.1 General information

Food allergy is an adverse immune reaction to food proteins. A number of factors determine why some people develop food allergy including individual susceptibility and dietary patterns. When food proteins are absorbed through the gut, they eventually interact with the immune system leading, in the majority of consumers, to the development of tolerance to the food. In genetically predisposed individuals, the interaction leads to sensitisation (i.e., the development of antibodies of the immunoglobulin E (IgE) class. The IgE molecules circulate in the body and attach to specialised cells called basophils and mast cells. Mast cells are present throughout the body and are prominent in tissues such as the skin, mucosa of the lungs and digestive tract, as well as in the mouth, eyes and nose. In a sensitised individual, the food proteins bind to the IgE attached to the mast cells triggering the release of chemical mediators such as histamine. The mediators interact with specific receptors present in various parts of the body, mainly the skin, throat, airways, intestines, and heart, leading to the symptoms of allergic reactions. IgE-mediated allergy, or type I hypersensitivity, is characterised by the rapid development of symptoms ranging from mild to life-threatening. Sensitisation, or the presence of food-specific IgE antibodies, is detected by testing the blood or skin of the individual. However, conclusive evidence of food allergy is achieved by double-blind placebo-controlled food challenge (DBPCFC) trials (Sampson, 1999 and 2003; Sicherer and Sampson, 2006).

Coeliac disease is an autoimmune-mediated condition triggered by dietary gluten in genetically predisposed individuals. It is also known as coeliac sprue, gluten-sensitive enteropathy, or nontropical sprue (Chang et al., 2009). The symptoms include abdominal bloating or pain, chronic diarrhoea and vomiting. Dietary exposure to gluten, the insoluble protein present in some cereal grains including wheat, barley and rye and their hybridised strains, triggers the symptoms in coeliac patients. Failure to eliminate gluten from the diet leads to chronic inflammation and damage to the lining of the small intestine. The tissue damage leads to nutrient malabsorption and possible serious complications including involvement of multiple organ systems and an increased risk of some malignancies (Sampson and Burks, 1996; Kagnoff, 2007, Presutti et al., 2007).

1.2.2 Food Allergy in Australia and New Zealand

The prevalence of food allergy in Australia and New Zealand is not known but it is estimated that 1-2% of the adult population and 4-6 % of the paediatric population are affected. Clinical data suggest that food allergy has increased in Australia, as in other countries, in the last decade. A study published in 2007 found a five-fold increase in the number of hospital admissions for food-induced anaphylaxis for zero to four year-olds and a four-fold increase for 5–14 year olds (Mullins 2007). The Australasian Society of Clinical Immunology and Allergy (ASCIA) estimates that 5% of Australian children will develop food allergy by school age.

1.2.3 Regulatory context

In the mid 1990s, food allergy was emerging as a significant public health issue in many countries around the world. As the processed food industry expanded and the volume of international trade in food products increased, the need for national and international regulatory control of food allergens became apparent. Allergen-specific avoidance diets were identified as critical for the safety of allergic consumers (Sporik and Hill, 1996; Hourihane, 1998). Recognising the importance of food allergy as a global issue for food regulation, the World Health Organization (WHO) and the Food and Agriculture Organization (FAO) sought expert advice to determine which foods should always be declared on food labels, because of their allergenic properties. A list of foods was developed based on frequency of severe reactions and estimated prevalence of allergic reactions. The advice was adopted by the Codex Alimentarius Commission in 1999 (Section 4.2.1.4 of General Standards for the Labelling of Prepackaged Foods) thus introducing labelling requirements for eight food allergens: cereals containing gluten, crustacea, egg, fish, peanuts, milk and tree nuts. A requirement for labelling of sulphites was also introduced. Although not typical allergens, sulphites can cause medically reproducible allergy-like reactions.

In Australia and New Zealand, allergen provisions were introduced into the Food Standards Code (the Code) in 2002. The Standard was based on advice from a panel of allergy experts from both countries. The expert panel was convened in 1997 by FSANZ to identify food allergens relevant to the Australia and New Zealand populations. The panel considered the prevalence and severity of allergic reactions to be the main criteria for identifying allergenic foods. The panel acknowledged that data on prevalence are often limited and defined 'severe' reactions as those which lead to significant morbidity and mortality. The panel advised that their clinical experience supports the foods listed by the Codex Alimentarius as frequent causes of severe systemic reactions. The Panel also recommended the inclusion of sesame seeds in the list based on clinical evidence that severe reactions to sesame products, including anaphylaxis, were increasing among infants (Sporik and Hill, 1996; Hill et al., 1997). The regulatory requirements were implemented with a two-year transition period and became fully enforceable in December 2002.

In the past few years, the United States of America, the European Union (EU), and Canada have also introduced regulations related to these eight foods and their products. The EU list also includes sesame seeds, celery, mustard, lupin, and molluscs. The Canadian list also includes sesame seeds and mustard.

As a result of the introduction of the allergen provisions in Standard 1.2.3, the listed foods are required to be declared on the label when present in food products. However, these regulations do not specifically address the unintended presence of these foods due to cross contamination. This is also the case in the regulations of the EU, USA and Canada.

There is currently no internationally agreed approach to the declaration of allergen cross-contamination. In June 2010, the European Parliament adopted an amendment that requires the development of common rules for labelling the presence of traces of allergenic substances. While drawing up such common rules is likely to be a complex and lengthy task, it may help improve the regulation of precautionary labelling of allergens.

2 Emerging food allergens

2.1 Allergenic foods – ‘the big eight’ and a few more

Any food that contains protein has the potential to cause allergic reactions in some individuals. It is not surprising then that at least 70 different foods have been reported to cause allergic reactions (WHO, 2006), and many more foods have been implicated (Hefle et al., 1996). However, the majority of allergic reactions reported in the medical literature in the past two decades are caused by only a small number of foods (Sampson and Burks, 1996; Hourihane, 1998). These foods are: wheat, peanuts, soybeans, milk, eggs, tree nuts, crustacea and fish. Known as the ‘big eight’, these foods account for 90 percent of all food allergies world-wide although regional and country specific differences exist.

While the vast majority of the population can consume these foods safely, very small amounts of these foods can cause serious, and potentially life-threatening, reactions in some individuals. Within the allergic population, individuals vary greatly in their response patterns to any food allergen. An individual’s sensitivity may change with time – for example, some individuals may become less sensitive or even ‘grow out’ of their allergy. Sensitivity may also increase due to an infection or due to uncontrolled asthma.

There is variation among allergenic foods in the amount required to cause an allergic reaction. The variation exists even between closely related foods such as peanut and soy. Allergenic foods may also vary in the severity of reactions they provoke in sensitised individuals. How much of a food is required to cause an allergic reaction and how severe the reaction is, are features that reflect the allergenic potency of the food (Björkstén et al., 2008). Allergenic potency is an important element of the management of the food allergy both at the individual and the population levels.

Cross-reactivity occurs among food proteins, particularly structurally similar or biologically related proteins. The IgE antibodies specific to one protein may bind to a similar protein in a different food. However, clinical reactions due to cross-reactivity are uncommon. There is currently no cure for food allergy, and allergen avoidance is the only option available to allergic consumers.

While the majority of the population are at no risk of food allergy, food labels provide essential information to allergic consumers to correctly identify food products which contain allergens they need to avoid. Due to the significant risks associated with food allergens, rigorous regulatory measures are warranted. However, the unique nature of food allergy risk, including the risk from accidental exposure to allergens due to unintended presence in food, is a challenge to the food industry and regulators.

2.2 Framework for the assessment of new food allergens

2.2.1 International approach

As discussed above, a number of foods have been recognised as important new food allergens at the country/ region level in addition to the ‘big eight’. These are: sesame in Australia and New Zealand, Canada and the EU; mustard in Canada and the EU; and celery, lupin and molluscs in the EU. These differences reflect population-specific factors such as diet and the reported incidence of allergic reactions in these regulatory jurisdictions.

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As food consumption patterns in the community change and new foods and ingredients enter the food supply, new allergens are likely to emerge.

Criteria for adding foods to the list of common allergenic foods were previously developed by an *ad hoc* Panel on Food Allergens for the Codex Alimentarius Commission. The panel recommended that the addition of a food to the list of common allergenic foods should be based on medical evidence that the food causes systemic reactions with typical features of allergic reactions and, where available, prevalence data in children and adults in several countries (WHO, 2000). However, the Codex list of priority allergens remains unchanged. Canada has recently developed criteria for the addition of new allergens which include the scientific recommendations agreed by the Codex Alimentarius Commission; the allergenic potency of the food or food ingredient (Björkstén et al., 2008), and the potential exposure to the food or food ingredient with specific consideration as to whether the food or food ingredient may become a hidden source of food allergens in pre-packaged food.

Also, the International Life Sciences Institute (ILSI) published a scientific paper proposing a revised set of criteria, including clinical considerations (diagnosis, potency of allergen, severity of reactions), population elements (prevalence, exposure) and modulating factors (food processing) (Björkstén et al., 2008; Løvik, 2009).

The purpose of the mandatory declaration list in the Food Standards Code is to prioritise the regulatory management of food allergens. Therefore, the guiding principle is that inclusion on the list should be determined by the public health significance of the food allergen of concern.

Since allergenicity is not an intrinsic, fully predictable characteristic of a food, premarket assessments such as those commonly used in toxicity assessments, are not applicable. Inevitably, scientific evaluations and any regulatory intervention will lag behind medical observations and reporting of allergic reactions in the community. This is particularly relevant for an emerging allergen where a period of time may lapse before clinical observations are disseminated and diagnostic testing is established. There is currently no systematic data collection on the frequency of allergic reactions to food in Australia and New Zealand.

Recent reports of severe reactions to lupin in Australia highlighted the need for a clear and transparent approach, including data requirements, to identify new allergens of importance in the context of food regulation. The approach is consistent with international criteria and relevant scientific information.

2.2.2 Data requirements to identify new allergens

FSANZ has identified the following data requirements to allow an evaluation of the population health significance of possible new allergens.

1. Evidence of cause-effect relationship, based upon positive DBPCFC.
2. Clinical reports of adverse reactions, with typical features of allergic reactions, following exposure to the food or its products.
3. Data on the prevalence and severity of allergic reactions to the food concerned in the Australian and New Zealand populations.
4. Information on and extent of use of the food and the range of products in the food supply in Australia and New Zealand.
5. Data on the allergenic potency of the food.
6. Where relevant, information on clinical cross reactivity with known allergens.

2.2.3 Sources of information

Data to support the evaluation of the public health significance of a new allergen is to be sourced ideally from the published literature. Where prevalence data are not available, information based on clinical records can be used to support the process of identifying food allergens of concern. In addition, FSANZ may seek direct input from allergy specialists and scientists with relevant expertise, as required.

2.3 Consideration of lupin as a new allergen

There is evidence that lupin is emerging as an allergen in Australia and lupin is increasingly used in food products in Australia. Here we provide a preliminary discussion and make a recommendation to further investigate the potential medical significance of lupin allergy.

2.3.1 Lupin allergy

Allergic reactions to lupin have been reported in the medical literature since 1994. More reports followed, mainly from Europe where lupin flour was increasingly used in food. The symptoms of lupin allergy are typical of severe Ig-E mediated allergic reactions and cases of lupin anaphylaxis have been reported by Matheu et al. (1999), Smith (2004), and Radcliffe et al. (2005). Lupin proteins show cross-reactivity *in vitro* with proteins from peanut and other legumes. The prevalence of lupin allergy is not known. Some peanut allergic individuals may also be allergic to lupin (Hefle et al., 1994; Moneret-Vautrin et al., 1999; Kim et al., 2007; Goggin et al., 2008; Shaw et al., 2008).

Lupin allergy was reported for the first time in Australia by Smith et al. (2004). The report, published in the Medical Journal of Australia, documented three cases of allergic reaction to lupin. The patients had reacted to food containing lupin flour, two requiring emergency care. None of the three patients was allergic to peanuts. The authors called for lupin to be included on the mandatory food allergy declaration.

FSANZ is aware that a few more patients have been diagnosed with allergy to lupin in Australia since 2004 (Dr William Smith, personal communications). To date, lupin allergy has not been reported in New Zealand.

Researchers in Australia sought to determine the clinical significance of lupin allergy among peanut sensitised individuals. The research aims to:

- Establish the prevalence of lupin allergy in peanut allergic individuals
- Identify lupin allergenic proteins
- Determine the relationship between lupin and peanut allergens

The research team is currently preparing the study for publication. FSANZ is communicating with the researchers to access the information as part of the risk assessment of lupin allergenicity.

2.3.2 Lupin in the food supply

Lupinus angustifolios, also known as Australian sweet lupin, is a major crop in Western Australia. Until recently, most of the Australian lupin crop was used for animal feed or exported to overseas markets. Now lupin is recognised for its high protein and fibre content as a valuable addition to the human food supply. Two other cultivated lupin species, *Lupinus albus* (white lupin) and *Lupinus luteus* (yellow lupin), are used widely in food in Europe.

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Trials of the yellow lupin are also underway in Australia. Lupin is related to other legumes, including peanuts and soy (Government of Western Australia, 2008).

In recent years, the use of lupin flour in food products has increased in Australia. The high protein and dietary fibre and low fat content of lupin make it attractive for human nutrition. Lupin flour and lupin bran are now used in a range of packaged and unpackaged food products such as pasta, bread, and bakery products. In addition, the Australian food industry sees a strong potential in the development and use of lupin-derived ingredients with potential use in dairy substitutes, sausage fillings (including vegetarian sausages), emulsions for salad dressings, baby food and diet products and scent and taste transporters. Lupin ice cream has already been introduced in Germany (Drake, 2008).

Information on the extent to which lupin is currently used in the food supply in Australia and New Zealand is not readily available. To address this information gap, FSANZ developed a research project in collaboration with Ms Alison Woo supervised by Professor Ken Buckle at the UNSW. The research provides evidence that a number of lupin-containing food products, either manufactured in Australia or imported, are available to consumers in Australia. In addition, lupin flour is used by bakeries in a variety of products, including bread, muffins and cakes. In New Zealand, it appears that, at this stage, lupin-containing products are not widely available to consumers (Woo – UNSW, 2008; NZFSA, personal communications).

FSANZ considers that information available on lupin allergy warrants further consideration through a proposal. This would allow FSANZ to formalise the process including the involvement of allergy experts and the public in discussions. Some members of the food industry have indicated their willingness to support such a proposal and would support the inclusion of lupin in the list of allergens in the Code.

One issue in particular that requires further discussion with stakeholders is the cross-reactivity between peanut and lupin, and the potential risk to peanut allergic consumers in Australia and New Zealand.

FSANZ has contacted a number of allergy specialists and scientists seeking their participation in a Scientific Advisory Group to discuss issues related to lupin allergy.

2.3.3 *Conclusions*

- Food allergy is a global issue that affects consumers, food manufacturers, health providers and regulators.
- The rigorous declaration requirements which apply to known presence of food allergens provide an effective risk management tool at the population level. These rigorous requirements are justified on the basis that such food allergens are of major public health significance.
- New food allergens may emerge that need to be considered for inclusion in the list for mandatory declaration. While the lists of food allergens may vary between countries, there is a need for an internationally consistent approach. Information requirements have been developed to underpin an evaluation of the significance of new allergens in a consistent and transparent manner.
- There is evidence that lupin is emerging as a food allergen in Australia. The significance of lupin allergy and cross reactivity with peanut needs to be evaluated by FSANZ.

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- As information available from the published literature on food allergy in Australia and New Zealand is limited, FSANZ will seek evidence and advice from allergy experts.

2.3.4 Recommendations

- FSANZ to establish a Scientific Advisory Group on food allergy and intolerance for consultations on relevant matters.
- FSANZ to develop a Proposal to consider whether an amendment to the Code to include lupin is justified.

3 Label information

Consideration of this issue has been broken down into two components. The first component relates to the clarity of information presented on the food label and, in particular, whether the source of the allergenic ingredient should be declared on the label. For example, should 'milk' be declared as the source of the ingredient 'casein' on the label. The second component related to the usefulness and accuracy of 'may contain' and similar precautionary labelling statements which refer to the possible inadvertent presence of the allergenic substance in the product. A useful source of information for the review is the recently completed consumer survey on allergen labelling (FSANZ, 2009), which provides an insight into consumer views and behaviour in relation to allergen labelling.

3.1 Source of allergenic ingredient

3.1.1 Australia and New Zealand

Clause 4 of Standard 1.2.3 – Mandatory Warnings and Advisory Statements and Declarations of the Code refers to the mandatory declaration on food labels of certain substances in food. The Table to clause 4 lists those substances that must be declared. These are: cereals containing gluten and their products, namely, wheat, rye, barley, oats and spelt and their hybridised strains; crustacea and their products; egg and egg products; fish and fish products; milk and milk products; peanuts and soybeans and their products; added sulphites in concentrations of 10mg/kg or more; and tree nuts and sesame seeds and their products. Although not explicitly stated in the text to clause 4, the substances listed in the Table to clause 4 are major food allergens, likely to cause adverse and potentially severe, reactions in some consumers. Clause 4 specifies which substances 'and their products' must be declared on a food label. However, it does not regulate the terminology to be used to identify these allergenic foods and their products.

Clause 4 of Standard 1.2.4 – Labelling of Ingredients, includes additional conditions relating to the declaration of some of the substances identified in Standard 1.2.3. Where the cereal is wheat, rye, barley, oats or spelt or their hybridised strains, then the specific name of the cereal must be declared. Where the source of the vegetable oil is peanut, soy bean or sesame, the specific source name must be declared. The specific names of the crustacea and nut present in a product must also be declared.

As a result of the current regulations covering the declaration of the major food allergens, the source of the ingredient declared on the label may not always be clearly stated, for example, ovalbumin, which is a product derived from egg. In addition, current regulations do not adequately meet consumers' needs for information on certain ingredients that can be derived from a number of different sources, of which not all are allergenic.

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An example is lecithin, which can potentially be derived from soy or rice, and maltodextrin, which can potentially be derived from wheat among other sources. In such circumstances, clearly stating the source of the ingredient may provide useful information regarding the substance to consumers who need to avoid the allergen in question in order to prevent life threatening adverse reactions. It may also help consumers avoid unnecessary restrictions in their food selection, where the source of the ingredient is non-allergenic.

3.1.2 *International regulations*

The Codex Alimentarius

The Codex General Standard for the Labelling of Pre-packaged Foods (CODEX STAN 1-1985) states that 'the following foods and ingredients are known to cause hypersensitivity and shall always be declared: cereals containing gluten; i.e., wheat, rye, barley, oats, spelt or their hybridized strains and products of these; crustacea and products of these; eggs and egg products; fish and fish products; peanuts, soybeans and products of these; milk and milk products (lactose included); tree nuts and nut products; and sulphite in concentrations of 10 mg/kg or more.' However, there is no prescriptive requirement for how to name the food source from which the allergenic ingredient is derived.

The European Union

The European Union (EU) directive (EU Directive 2003/89/EC amending 2000/13/EC) makes it mandatory for the food industry to list 12 potential food allergens on the product labels regardless of the quantity in the finished product. The regulations state: 'The list of allergenic substances should include those foodstuffs, ingredients and other substances recognised as causing hypersensitivity'. Again, there is no specific requirement as to the terminology to be used to declare the substance.

The United States of America

In the United States, the *Food Allergen Labelling and Consumer Protection Act 2004* (FALCPA) of the US Food and Drug Administration (USFDA) mandates manufacturer disclosure of the most common allergens (milk, egg, wheat, soy, peanut, tree nuts, fish and crustacean shellfish) in plain English, using the common or usual name, in the ingredient list or in a separate allergens summary statement. The name of the food source from which the allergenic substance is derived is required e.g. 'milk casein'. In addition, FALCPA mandates the disclosure of the type of tree nut, fish or crustacean shellfish.

A recent audit of manufactured products (Pieretti, 2009) for use of allergen labelling statements identified only a very small percentage of products with FALCPA violations involving the use of non-food source terms, for example, 'whey' without the term milk, 'durum flour' without the term 'wheat'.

From the results of this audit, it appears that regulating for the declaration of the source of allergen has been a successful means of ensuring that food manufacturers provide adequate information on the label about allergenic ingredients. Given the high level of compliance in the US (and given current labelling practices in Australia which indicate that manufacturers are already meeting these requirements, as discussed further on), results may also suggest that should such a regulatory approach be implemented by FSANZ, it may not pose undue difficulties for manufacturers to implement.

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Pieretti (2009) identified several labelling ambiguities which may present areas of potential confusion for the individual with food allergy. One of the main issues, that has already been outlined in 3.1.1 above, involved the declaration of ingredients that may have allergenic or non-allergenic sources. Given that non-allergenic sources are not required to be qualified in Australia and New Zealand this requires a relatively sophisticated understanding of the labelling requirements by consumers.

3.1.3 Outcome of stakeholder consultation

In March 2008, FSANZ released an issues paper for targeted stakeholder consultation. The paper outlined the issues that FSANZ intended to cover in the review, sought comment on these and requested information to inform the review. Submissions were received from approximately 20 key stakeholders representing jurisdictions, the food industry, consumer support groups and health professionals. Responses to the issues paper revealed general support for the need for clarification of terms in the Code. In particular, there was support for the source of ingredients to be declared, with stakeholders proposing that this would involve the replacement of terms such as *ovalbumin* with *egg* and *casein/ whey* with *milk*. The comment was also made that they understood that the original intent of the mandatory declaration of allergens under clause 4 of Standard 1.2.3 was for common names to be used. However, the drafting of the current standard had left this aspect open to interpretation.

There was also support for the need to clarify the source of ingredients that may have been derived from alternative sources, not all of which are allergenic, for example lecithin (as previously mentioned) and thickener, (which can be derived from wheat, or from other non-allergenic sources such as maize).

3.1.4 Consumer research

Two surveys examining consumers' perspectives in relation to allergen labelling have been undertaken by FSANZ as part of the FSANZ Evaluation Strategy.

The first survey, a benchmark study conducted in 2003, collected baseline data on consumers' views and behaviours towards the then newly introduced food allergen labelling requirements (FSANZ, 2004). A follow-on survey was conducted in 2008, largely replicating the measures from the benchmark survey (FSANZ, 2009). The aim of the follow-on study was to provide an indication of the current situation as well as a comparison to practices in 2003 when the changes to allergen labelling provisions were only just being implemented.

The benchmark survey found that many people with food allergies, when presented with a list of substances, did not recognise all of the terms used to describe the allergenic substances. For example, a large percentage of those with a wheat allergy did not recognise that thickener, semolina, couscous, cornflour, starch, icing sugar mix, textured vegetable protein and maltodextrin could all potentially contain wheat.

The follow-on survey noted that the rate of recognition of many ingredients and products has increased in 2008 compared with 2003. However, a number of ingredients are poorly recognised when the source is not included. For example, among milk allergic individuals 81% identified lactose, 76% identified butterfat, 73% identified casein and 71% identified whey as words that indicated the presence of ingredients of concern to them. Although the risk to the consumer varies according to their sensitivity and the allergenic content of the ingredient, and therefore personal judgement and experience play a major role in decision making, clearly some consumers are unable to identify ingredients of concern.

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The industry guideline on allergen labelling, discussed below, recommends the use of clear and easy to understand terms in association with the ingredient.

Overall, there were improvements in the area of label clarity in 2008 compared with 2003. However, results indicate potential risk to allergic consumers who do not recognise ingredients of concern. Less than half of the respondents agreed that it was easy to understand and use food labels.

In particular, respondents reported that the use of many or different names for the same ingredient was a problem for them, making it difficult to select appropriate food products and avoid the allergens of concern. This was reflected in their suggested improvements to labelling, where comments centred around the need to be more specific as to the types and source of ingredients such as vegetable oil, emulsifiers, thickeners etc. Similar issues were identified in a recent European study examining food allergic consumers' preferences for labelling practices. The study, which included 40 participants, reported that the ingredient list was considered incomplete and the information not sufficiently specific (Voordouw et al., 2009).

It should be noted that despite the call for further clarity and detail in the ingredient information provided on labels, there does not appear to be any evidence of this as a cause of allergic reactions. In response to an open-ended question, 5% of respondents reporting a serious reaction since the allergy was first identified said this was due to *unlabelled or incorrectly labelled* food. Consumer comments did not indicate any specific deficiencies in relation to the clarity of information as being a cause of a repeat allergic reaction. However in response to a separate question, lack of clarity of information about the allergenic ingredient was not reported as being a cause of a repeat allergic reaction.

3.1.5 Food industry initiatives

In 2005, the Allergen Bureau¹ was established as an industry funded resource providing information and tools to improve awareness and skills in relation to allergens in the food manufacturing environment. The Australian Food and Grocery Council (AFGC) published the 'Food industry guide to allergen management and labelling (revised edition)' in 2007, providing guidelines on the management of allergens in the food processing environment and recommended labelling formats (AFGC, 2007). The aim of the industry guide is to promote the declaration of allergen information on food labels in a clear and consistent manner to enable food allergic consumers and their carers to easily determine the suitability of particular foods. The guide recommends that:

- all allergen information should be grouped together to be easily identified and not hidden amongst other labelling information
- product description and representation should provide an accurate expectation of the product and should not be misleading
- allergens must be declared using plain English terms consistent with the Code
- the print size should be big enough to be easily read, preferably at a minimum 1.5mm with sans serif font, and the font colour should contrast distinctly from the background.

¹ The Allergen Bureau was established in 2005 as an initiative of the AFGC Allergen Forum to provide information, practical tools and contacts for the food industry to improve the management of food allergens and derived ingredients. Non-industry participants include food regulators, allergy experts and allergy support groups.

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- the use of lower or upper case will depend on the overall presentation of labelling information.

The recommended labelling format consists of an ingredient list declaring allergenic ingredients and their derivatives in bold, an allergen summary statement, and a precautionary statement. The ingredient/ component should be qualified according to the allergenic foods listed in the Table to clause 4 of Standard 1.2.3, either in the ingredient list itself or in the allergen summary statement. This is to ensure that the allergenic ingredients are clear to the sensitive consumer, through use of the source name. Implementation of the guide by food manufacturers is voluntary.

3.1.6 Label monitoring surveys

Label survey information that gives an indication of the state of allergen labelling is useful to complement the information gathered in consumer surveys on how consumers are perceiving allergen labelling, its usefulness and limitations. Such information is available from various sources including label monitoring surveys conducted by FSANZ and the food industry.

3.1.7 FSANZ label monitoring surveys

Food label monitoring surveys have been undertaken by FSANZ since 2002. These surveys provide an indication of current allergen labelling practices, the results of which can complement the consumer information gathered.

Food label monitoring surveys were undertaken in 2002/2003 (Phase 1) and again in 2005/2006 (Phase 2). Surveys were conducted to assess how food manufacturers were managing key labelling requirements. In any one year of the survey, between 1200-1300 food labels were collected from 14 different food categories in Australia and New Zealand and assessed for consistency with the Code.

Phase 1 was undertaken during a period of transition to the new Code and shortly thereafter. Phase 2 was undertaken when changes to the allergen labelling provisions had been in full effect for several years. Each label was assessed against twelve key labelling elements, including allergen labelling.

In Phase 1, an assessment of allergen labelling covered legibility only. All labels assessed in Phase 1 were assessed as legible and therefore consistent with the requirements of the Code (FSANZ, 2004). In Phase 2, the methodology was altered to include an assessment of whether ingredients were accurately qualified, for example, flour qualified with the cereal type (FSANZ, 2008). In Phase 2, a small number of labels were assessed as inconsistent with this criterion, with the most common inconsistency being failure to qualify the cereal/ flour with the cereal type.

The results of Phase 1 indicate that the most common method of declaring the presence of allergens was in the ingredient list, rather than elsewhere on the label, and using the common/source name rather than a technical term. This apparent trend continued in Phase 2, with virtually all labels declaring the presence of allergens in the ingredient list. Use of common/source names was again high.

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3.1.8 FSANZ allergen label monitoring survey

Information on the extent of application of the industry guide to allergen management by the food industry would be useful to complement information gathered by FSANZ through the food label monitoring surveys.

In 2009, FSANZ undertook a label monitoring survey focusing on allergen declaration. The survey analysed 182 labels containing allergen declarations, to assess allergen label information on products in Australia against the allergen labelling provisions in the Code as well as the labelling recommendations set out in the industry guide. As in Phase 2 of the label monitoring survey discussed above, (99%) of these products were assessed as consistent with the Code's Standards 1.2.3 and 1.2.4. Only two cases of allergen labelling were found to be inconsistent with the Code, due to failure to qualify the flour with the cereal type. Thirty-four percent of labels were assessed as consistent with all of the labelling recommendations set out in the industry guide.

As noted in previous surveys, the most common method of declaring the presence of allergens was in the ingredient list, rather than elsewhere on the label. In some cases the ingredient was declared, for example, 'casein', but in direct association with the source (e.g. 'milk casein' or 'casein (milk)'), or else the ingredient was declared in the ingredient list, with the source declared in a separate summary statement (e.g. 'this product contains milk').

Less than one in ten labels did not clearly state the source/ common name, either in the ingredient list or in a separate allergy statement. These labels included the terms 'cheese', 'cream' and 'butter' (instead of 'milk'), 'gluten', 'cereal/ flour' (instead of the specific cereal such as 'wheat'), 'nut' (instead of 'tree-nut' or 'peanut'), 'salmon' (instead of 'fish'), and 'shrimp' (instead of 'crustacea').

3.1.9 Allergen Bureau labelling review survey 2009

An allergen labelling survey of 340 packaged retail food products with allergen declarations was carried out by the Allergen Bureau in 2009. This survey followed on from an earlier survey of 213 labels also undertaken by the industry in 2005.

The aim of the second survey was to provide information on how allergen related information is currently being declared on food labels, compared to the recommended labelling formats set out in the industry guide (Allergen Bureau, 2009).

Reflecting the results of FSANZ's surveys, the most common method of declaring the presence of allergens was in the ingredient list, rather than in a summary statement or as a separate claim elsewhere on the label. As previously stated, the industry guide recommends that the ingredient/ component be qualified according to the allergenic foods listed in the Table to clause 4 of Standard 1.2.3. An assessment of this aspect would provide an indication of the extent of use of the source name (as opposed to ingredient names or technical names). This aspect was not measured directly, but the use of plain English terminology across the two surveys, was around 96% of labels that had allergens declared in the ingredient list. From these results, the authors contend that this aspect is being addressed adequately by the majority of food manufacturers surveyed.

Together with the results of the recent label monitoring surveys conducted by FSANZ, these results support the view that food manufacturers are making efforts to adhere to industry guidelines, in declaring the source of the ingredient, either in the ingredient list or in a separate allergen summary statement. As such, the need for added regulation in this area would not appear to be imperative.

3.2 Precautionary labelling

3.2.1 Allergen cross contact

The purpose of precautionary labelling is generally to alert food allergic consumers to the possible presence of an allergen in the product where the allergen was not intentionally added but may have occurred due to cross contact. The cross contact may result in significant or only trace amounts of an allergenic substance that are sporadically introduced to the food products. Cross contact may occur anywhere along the supply chain and/or the production process including the growing and harvesting of crops, storage and transport of food, or via processing equipment at the manufacturing plant.

Whilst the current allergen declaration requirements in the Code do not prohibit the use of precautionary statements such as 'may contain...', the Code does not include specific provisions for food labelling in relation to cross contact allergens. To provide additional information to consumers on the possible presence of allergens due to cross-contact food manufacturers started using a variety of precautionary statements such as:

'may contain...'

'may contain traces of...'

'made in the same premises as products containing...'

'made on the same equipment as products containing...'

Allergic consumers and public health professionals have criticised the food industry for inconsistent and an apparent 'blanket approach' to precautionary allergen labelling. Data from consumer surveys indicate that there are a significant percentage of allergic consumers who do not always heed the precautionary statement and therefore may be taking risks by choosing to consume these products.

3.2.2 International regulations

FSANZ is aware that other food regulators are also considering the issue of precautionary labelling.

The Japanese Ministry of Health, Labour and Welfare is the only known agency that, under its Ministerial Ordinance on the Food Sanitation Law Enforcement Regulations, currently forbids the use of 'may contain' labelling. However, statements such as 'made on the same equipment as products containing...' are deemed acceptable for use.

Precautionary labelling is not currently regulated in the EU and the USA. The Canadian government (Health Canada) is in the process of reviewing its policy on the use of precautionary statements for food allergens. The policy review will focus on identifying specific statements that industry will be allowed to use on labels, as well as conditions that must be met before they are allowed to use these statements.

In August 2008, the USFDA held a public hearing on the use of precautionary labelling of allergens in foods, with the aim of developing a long-term strategy to support manufacturers in using precautionary labelling that is truthful and not misleading, conveys a clear and uniform message, and adequately informs food-allergic consumers and their caregivers. The public hearing was a first step in collecting information on how manufacturers are currently using precautionary labelling, how consumers interpret the different precautionary statements and their perceived usefulness, and what wording is likely to be most effective in communicating to consumers the likelihood that an allergen may be present in the food. The outcomes of the public hearing will support the USFDA in its consideration of various government and industry approaches to develop its precautionary labelling guidelines.

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There is no information available in relation to the timelines of the USFDA's development of precautionary labelling guidelines.

3.2.3 Outcome of stakeholder consultation

Responses to the issues paper released by FSANZ in March 2008 for targeted stakeholder consultation indicated that precautionary labelling and, in particular, the plethora of various statements currently being used, was an area of concern. Consumers may not be able to evaluate the actual risk through these statements alone, and could misinterpret the potential harm that the food in question may cause.

There was support for voluntary, industry based initiatives in this area (see section on *Food industry initiatives* below), and the comment was made that FSANZ could participate and support the further development of these industry based strategies rather than seek to achieve similar outcomes through mandatory regulation.

3.2.4 Food industry initiatives

The industry guide specifically addresses cross contact allergens through the Voluntary Incidental Trace Allergen Labelling (VITAL) system. VITAL, launched in June 2007, aims to provide a risk-based approach for food manufacturers to use in assessing the impact of cross contact allergens and to guide the use of appropriate allergen advisory labelling (AFGC, 2007). The Allergen Bureau continues to further develop VITAL and provide training to food manufacturers on its application.

VITAL uses a decision tree and action level grid, which identifies three action levels, to determine the need for precautionary labelling. The VITAL action levels are:

- Action Level 1 – Green Zone – precautionary labelling is not required for the allergen under evaluation.
- Action Level 2 – Yellow Zone – precautionary labelling is required for the allergen under evaluation, using the recommended precautionary statement 'may be present: xxx' where 'xxx' lists each of the cross contact allergens present at VITAL action level 2. The precautionary statement 'may be present' is to be used only in conjunction with VITAL.
- Action Level 3 – Red Zone – significant levels of the allergen are likely to be present in the food; therefore, listing the allergen in the ingredient list is required.

The VITAL Action Levels are based on the principle that there is a lower limit of allergenic food which triggers an allergic reaction. The VITAL levels use currently available information, from the published literature, on the lowest observed adverse effect levels (LOAELS). Research is continuing, mainly in Europe, to improve the quality and quantity of data in this area of clinical testing for the purpose of establishing threshold levels for allergenic foods. The VITAL system is to be periodically reviewed to ensure it remains up to date, with the first review currently underway.

The Allergen Bureau has also developed a product information form (PIF) for use by companies to collect information about the origins of ingredients, including their composition and the presence of allergens, amongst other information. The allergen information contained in the PIF can be incorporated into the VITAL decision tree to assist in determining the appropriate VITAL action level.

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The Allergen Bureau provides training on the use of the VITAL system and PIF to the food industry. FSANZ, through its participation in meetings and conferences, remains aware of industry efforts and progress in this area. The New Zealand Food and Grocery Council (NZFGC) endorses industry initiatives implemented by the AFGC in Australia regarding the management of allergens in the food processing environment, and makes the 'Food industry guide to allergen management and labelling' (AFGC, 2007) available via its website.

3.2.5 Consumer research

Consumer research (2003 and 2008) collected data on consumers' views and behaviours towards food allergen labelling requirements, including the use of precautionary labelling statements. Both surveys indicated that the extensive use of precautionary labelling presents a difficulty to allergic consumers and their carers. A main concern was that precautionary statements were overused, possibly by manufacturers 'when in doubt'. The overuse of precautionary statements may cause allergic consumers to unnecessarily restrict their food choices, and undermines the impact of the statement. Studies have shown that food allergic consumers may ignore product precautionary statements as a result of an increase in use of such statements (Hefle et al., 2007; Lemon-Mule *et al.* 2007). A further concern was that due to the ambiguous wording of many precautionary statements such as 'may contain...', such statements carry with them a level of uncertainty such that consumers cannot be assured one way or the other about the presence of the allergen.

The most recent consumer research (FSANZ, 2009) also indicated that consumer understanding and behaviour in response to precautionary labelling varied widely depending on the statement. Questionnaire respondents were presented with the following precautionary statements:

'may contain traces of...'
'made in the same premises as...'
'made on the same equipment as...'
'may be present'

The final statement 'may be present' was not included in the original benchmark survey questionnaire, but was added to the follow-on survey questionnaire following its introduction via the industry based initiative VITAL.

For all four statements, between one third and one half of respondents considered them to be 'not very useful'. These results represented an improvement since 2003, where over one half of respondents considered the first two statements to be 'not very useful'. In both surveys, the statement 'made on the same equipment as...' was considered the most useful, with 46% and 34% of respondents considering this statement to be very useful in 2003 and 2008, respectively.

In terms of avoidance, in both surveys, most respondents would either always avoid or sometimes avoid products featuring these statements. The likelihood of always avoiding the product varied somewhat, depending on the statement type, with 66% and 47% of respondents always avoiding a product labelled with 'made on the same equipment as...' according to the 2003 and 2008 surveys, respectively.

The highest level of avoidance occurred in response to the precautionary statement 'may be present' which is recommended in the AFGC Guideline (AFGC, 2007). Sixty percent of respondents reported always avoiding a product labelled with 'may be present'. The statement 'may be present' is recommended in the AFGC Guideline in conjunction with the application of the VITAL system.

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This is an interesting result given the recent introduction of VITAL and this particular statement. This result appears to be a spontaneous reaction by consumers to the wording of the statement and may not relate to the level of consumer awareness of the VITAL system that underpins the use of the 'may be present' statement. The survey did not provide respondents with any information regarding the VITAL system, nor was any prior knowledge and awareness of this system among respondents assumed. However, this is a promising start as it indicates that the choice of wording of the statement itself appears to have an instinctive effect on consumers compelling them to avoid the product.

In relation to the various precautionary statements, it appears that consumers are assigning differential levels of risk to differently worded precautionary statements, in the absence of further information. The statement 'made on the same equipment as...' was considered the most useful, possibly because it is less ambiguous than the other statements evaluated, and it describes an actual processing step where cross contact with allergens may occur. However, allergic consumers are less likely to avoid products with this statement than products with 'may be present' statement.

3.2.6 Label monitoring surveys

FSANZ label monitoring surveys

Label monitoring surveys have been commissioned by FSANZ since 2002 to assess how food manufacturers are managing key labelling requirements set out in the Code. Correct labelling is a key objective of the *Food Standards Australia New Zealand Act 1991* to ensure consumers have adequate information to help them make informed choices.

The results of these surveys have assisted FSANZ in assessing the effectiveness of current labelling regulatory measures and also provide evidence to inform future decisions on labelling laws, as part of the standards development process.

Food label monitoring surveys undertaken by FSANZ in 2002/2003 (Phase 1) and 2005/2006 (Phase 2) examined the use of precautionary labelling statements as part of allergen labelling requirements.

A plethora of statements was reported, with the most common statement being 'may contain traces of...'. Other commonly used statements included 'may contain X traces', 'this product may contain traces of...', 'may contain...', and 'manufactured on equipment that also produces products containing...'. Analysis of the most recent (Phase 2, 2005/2006) indicates that precautionary labelling statements were present on 28% of labels assessed.

The table below provides a breakdown of the different wordings used for precautionary statements.

Percentage of labels	Wording of Precautionary Statements
59%	' May Contain Traces'
7%	'May Contain...' (Note the word traces is not used)
29%	'Made/manufactured in equipment/factory/facility that also packs/comes into contact with...'
5%	Other

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It should be noted that the Phase 2 survey was undertaken in 2005-2006, prior to the launch of the food industry guidance on precautionary labelling.

FSANZ allergen label monitoring survey

The allergen label monitoring survey undertaken in 2009 examined the use of precautionary labelling statements against the labelling recommendations set out in the industry guide. Precautionary labelling statements were present in 48% of labels (88 of 182 labels) collected and covered all of the major food allergens, noting that in this survey, labels were selected on the basis of there being either an allergen declared in the ingredient list; an allergen summary statement; or a precautionary statement.

Thirty-five different precautionary statements were recorded, representing variations of the statements given in the table below.

Percentage of labels	Wording of Precautionary Statements
41%	'may contain traces of...'
15%	'may be present'
13%	'made/manufactured on equipment/machinery that also processes...'
9%	'made in a facility/plant that also processes products with/containing...'
9%	'may contain...'
13%	other

Note that the industry recommended wording 'may be present' was used on 15% of labels with precautionary statements.

Allergen Bureau labelling review survey 2009

The labelling review survey undertaken by the Allergen Bureau in 2009 examined allergen related information on 340 packaged food products. Results were similar to those obtained in the FSANZ mini allergen label monitoring survey also conducted in 2009. In this survey, precautionary labelling statements were present on 47% of sampled products. Thirty-four different precautionary statements were recorded, with the most frequently used precautionary statements shown in the table below.

Percentage of labels	Wording of Precautionary Statements
38%	'may contain traces of...'
7%	'may be present'
22%	'manufactured/made on equipment/production line that also processes...'
6%	'may contain...'
1%	'contains traces of'
26%	other

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The industry recommended precautionary statement 'may be present' was used on 7% of labels with precautionary statements.

In summary, the results of label monitoring surveys examining the use of precautionary labelling statements indicate that the use of a broad range of statements continues. At this time, uptake of the recommended wording 'may be present', appears to be limited. This is understandable as the management of allergens by food manufacturers to reduce the need for precautionary labelling is a complex task and the industry initiative is still at an early stage of implementation.

The VITAL system involves a series of technical steps including assessment of the likely sources of allergens from raw materials and the processing environment, evaluation of the amount of allergen present, determining the ability to reduce the allergenic material from all contributing sources as well as ongoing monitoring and verification. The Allergen Bureau is committed to improving precautionary labelling practices across the industry. The Allergen Bureau has made recommendations for future work to increase the number of food manufacturers following the industry guide.

While this voluntary system is underway in Australia and New Zealand, there remains a gap with regards to imported foods, where the same or equivalent measures are not adopted by the country of export.

3.3.1 Conclusions

- The use of clear terminology and easily understood names for ingredients assists allergic consumers in recognising products they need to avoid.
- Despite improvement in consumers' ability to recognise ingredients of concern where the source allergen is not declared by name, a percentage of allergic consumers fail to do so. However, data from the label monitoring surveys indicate that declaration of the source of allergenic ingredients is widely practiced by the food industry on a voluntary basis, as recommended by the peak industry body the AFGC and endorsed by the NZFGC.
- In general, regulatory requirements and additional voluntary declarations provide adequate information to allergic consumers to assist them in identifying ingredients of concern. Based on the consumer survey of 2009, 5% of respondents reported they have suffered an allergic reaction due to unlabelled or incorrectly labelled food.
- Allergic consumers and their carers have an expectation that precautionary labelling should be truthful and not misleading, and provide accurate, clear and consistent information about the potential presence of food allergens.
- FSANZ recognises that the potential for cross contact allergens is inherent to the food production and processing environment. A desirable outcome is to improve the precautionary labelling such that it maximises food choices for allergic consumers without compromising safety.
- Precautionary labelling is recognised internationally as a difficult area to regulate. The science needed to answer relevant questions and to underpin decisions, such as allergen thresholds and the reliability of detection methods, is not available or is incomplete. Research is continuing to improve the evidence base and to establish robust risk assessment methodology in this area.

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- The food industry is committed to improving the management of food allergens along the supply chain and in the manufacturing environment. A voluntary approach to precautionary labelling is endorsed by industry peak bodies in Australia and New Zealand.
- The initiative by the food industry to improve the management of cross contact allergens and the use of precautionary labelling is currently underway. FSANZ recognises the commitment by the food industry to improving the use of precautionary labelling through the development and adoption of strategies to minimise cross contact. The adoption and consistent application of these tools has the potential to address the issue of precautionary labelling without the requirement for mandatory regulation in this area.
- The effectiveness of the voluntary system could be enhanced further by information programs for consumers on the correct use and meaning of the recommended precautionary labelling statement
- While the application of the VITAL system is expected to improve the use of precautionary labelling for food products made in Australia and New Zealand, a gap remains with regards to imported foods, where similar voluntary measures are not adopted by the country of export.

3.3.2 Recommendations

- FSANZ to continue working with industry to support a voluntary system to improve the use of precautionary labelling through management of allergen cross contact.
- In collaboration with the food industry, FSANZ to put in place a label monitoring program specifically designed to track improvements in allergen labelling practices with a particular focus on 'source' and precautionary labelling. The data gained would allow FSANZ to track the effectiveness of voluntary practices and would assist the industry in achieving its goal to provide accurate, useful information to allergic consumers.
- FSANZ will consider the outcomes of reviews currently underway by overseas regulatory authorities on precautionary labelling.

4 Foods Exempt from Bearing a Label

It is recognised that many of the allergic reactions that occur in the population are attributed to unlabelled food eaten outside the home (Bock et al., 2001; Anaphylaxis Australia, 2008; Allergy UK, 2009), such as in restaurants and cafes. FSANZ was aware of a number of allergy support groups and enforcement agencies that provide allergy education and support for the food service sector. As part of this review FSANZ undertook an evaluation of the adequacy of the current regulatory requirements relevant to food exempt from bearing a label, in addition to non-regulatory measures, in meeting the needs of food suppliers and food allergy sufferers.

As part of the targeted consultation process, FSANZ sought stakeholder views on the adequacy of current mandatory declaration requirements. Also sought were suggestions on how food suppliers could better communicate allergen information to consumers.

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FSANZ also sought information on non-regulatory initiatives aimed at reducing the incidence of allergy caused by food purchased and/or consumed in food service establishments.

Currently, Standard 1.2.1 – Application of Labelling and Other Information Requirements of the Code, requires that foods for retail sale that are exempt from bearing a label² must comply with the specific allergen information requirements as set out in clause 4 of Standard 1.2.3. Clause 4 of Standard 1.2.3 mandates that where the food is exempt from bearing a label, food allergens when present as an ingredient, an ingredient of a compound ingredient, a food additive, or a processing aid must be declared on or in connection with the display of food; or declared to the purchaser upon request.

In responding to the question on the adequacy of the mandatory requirements seven stakeholders indicated that they were satisfied with the current requirements (Allergen Bureau, Allergy Unit Adelaide, Confectionary Manufacturers of Australasia Limited, Dept of Health WA, Environ Health Office Qld, Manufactured Food Database, NZFSA) and three (Dietitians Association of Australia, Allergy New Zealand, Anaphylaxis Australia) indicated that they were not satisfied.

The stakeholders who were not satisfied with the current requirements in the Code were of the view that:

1. there is limited evidence to suggest that this sector has an adequate understanding of their obligations in relation to the Code
2. the current exemptions for food for catering purposes allows for the possibility that staff in retail premises do not have sufficient information regarding the allergen content of the food they are preparing.
3. the risk of cross contamination is not addressed in the Code; nor is there clarity around the time frame within which allergy information should be declared following a request from the purchaser.

In general, stakeholder responses indicated that there were several groups involved in providing resources or implementing new initiatives to enhance the knowledge of the staff in the food service sector in relation to allergens. Two stakeholders also indicated the importance of getting Restaurant and Catering Australia and Restaurant Association of New Zealand to be part of any educational activity FSANZ may consider. Overall there was an indication of the need for more effective means of communicating regulatory obligations and the establishment of further education and training for staff at all levels in this sector.

Subsequent to the targeted stakeholder consultation, FSANZ gathered information on the educational initiatives conducted by Anaphylaxis Australia, Allergy New Zealand, the Allergen Bureau and the Jurisdictions responsible for enforcing the Code in Australia and New Zealand. The consultation included an assessment of the communication methods used to inform local enforcement bodies and food businesses on the regulatory requirements for allergens. This work indicated that Anaphylaxis Australia, Allergy New Zealand, and the Allergen Bureau have completed several educational activities in this area and are also progressing new initiatives.

In relation to the activity of jurisdictions there were guidelines and policies established by most jurisdictions for the management of anaphylaxis in the school setting. Some Jurisdictions also offered allergen management training support specific to school settings.

² For example unlabelled delicatessen food and food sold at restaurants.

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However in overall terms only some jurisdictions were proactive in establishing initiatives to communicate the regulatory obligations and enhance the knowledge of workers in the food service sector. For example Department of Human Services Victoria and the New South Wales Food Authority have initiated pilot projects for training hospitality staff about food allergies and intolerances and NZFSA has included the training of staff in relation to allergens as part of the implementation of requirements for food businesses to have Food Control Plans.

FSANZ is not aware of any quantitative data on the number of cases of anaphylaxis related to non-compliance of the Code or non-disclosure of specific information as required by the Code. Based on the information currently available, it is FSANZ's view that the current regulatory measures are adequate to manage the food allergy risks from food exempt from bearing a label. However, there is a need for establishing more effective means of communicating these regulatory obligations and implementing initiatives to enhance the allergen management knowledge of workers in the food service sector. FSANZ considers the jurisdictions are best placed to communicate the regulatory obligation and provide access to educational initiatives and we would be pleased to work with jurisdictions in facilitating this process as required. It is recommended that these views be presented to the Implementation Sub Committee (ISC) for their consideration.

4.1.1 Conclusions

- Many of the allergic reactions that occur in the population are attributed to unlabelled food eaten outside the home, such as in restaurants and cafes.
- The majority of the stakeholders who were consulted are satisfied with the current allergen related mandatory requirements in the Code specific to foods exempt from labelling.
- There are several groups involved in providing resources or implementing new initiatives to enhance the knowledge of the staff in the food service sector in relation to allergens. However overall there is an indication of the need for more effective means of communicating regulatory obligations and the establishment of further education and training for staff at all levels in this sector.
- In relation to the educational initiatives, Anaphylaxis Australia and Allergy New Zealand have completed several educational activities in this area and are also progressing new initiatives.
- Only some jurisdictions are proactively establishing initiatives to communicate the regulatory obligations and enhance the knowledge of workers in the food service sector.
- FSANZ is not aware of any quantitative data on the number of cases of anaphylaxis related to non-compliance of the Code or non-disclosure of specific information as required by the Code.
- It is FSANZ's view that the current regulatory measures are adequate to manage the food allergy risks from foods exempt from bearing a label. However, there is a need for establishing more effective means of communicating these regulatory obligations and implementing initiatives to enhance the allergen management knowledge of workers in the food service sector.

4.1.2 Recommendation

- With respect to allergen declarations in the food service sector, it is recommended that the Implementation Sub Committee be asked to consider the communication of regulatory obligations to food businesses and to provide access to educational initiatives, with FSANZ assistance as required.

5 Labelling requirements for the current list of allergens

The current list of allergens in the Code was developed in the late 1990s based on information available at the time. Since then, scientific and clinical research in the area of food allergy has intensified. FSANZ, in consultation with stakeholders, has identified a number of issues relating to the current requirements which could benefit from the research outcomes. These issues are: identifying tree nuts of clinical significance in the context of allergy; evaluating the term 'fish' as defined in the code and its usefulness to stakeholders; the distinction between wheat allergy and gluten-related adverse reactions.

5.1 Collective term 'tree nuts'

Table to clause 4 of Standard 1.2.3 requires the declaration of tree nuts but does not specify the tree nuts known to be significant allergens in Australia and New Zealand. Schedule 4 of Standard 1.4.2, includes a list of sixteen '**tree nuts**' These are: almonds; beech nuts; Brazil nuts; cashew nuts; chestnuts; coconut³; hazelnuts; hickory nuts; Japanese horse-chestnut; macadamia nuts; pecan; pine nuts; pili nuts; pistachio nuts; sapucaia nut; and walnuts. Standard 1.2.4 – Labelling of ingredients – requires the specific name of the nut must be declared.

FSANZ's stakeholders, including consumers and food manufacturers have frequently sought clarification on the specific tree nuts that are allergenic and therefore, subject to the mandatory declaration requirements of Standard 1.2.3.

5.1.1 Tree nut allergy

Tree nuts have been reported in the medical literature to cause severe allergic reactions in children and adults. Hill et al. (1997) estimated the prevalence of tree nut allergy in Australian children to be 0.76%. Based on studies by Sicherer et al. (1999; 2003 and 2010), the prevalence of childhood tree nut allergy in the US has increased significantly in the past decade. Data from three telephone surveys conducted over a ten-year period estimates the prevalence as 0.2% in 1997, 0.5% in 2002 and 1.1% in 2008. In Canada, the prevalence of probable allergy to tree nuts was estimated to be 1.14% (Ben-Shoshan et al., 2010).

Tree nuts are among the most frequently implicated food in anaphylaxis (Sampson, 2000). In the United Kingdom, 15 out of the 37 food-induced fatalities recorded from 1992 to 2000, were due to tree nuts (Pumphrey, 2000). A report on fatalities due to anaphylactic reactions to food in the USA identified tree nuts as the cause in 27% of cases (Bock et al., 2001). In Australia, four cases of fatal anaphylaxis due to tree nuts were reported in 1998-1999 in a single adult emergency department in Brisbane, Queensland (Brown and McKinnon, 2001).

³ Coconut is currently excluded from mandatory declaration requirements in Standard 1.2.3 of the Australia New Zealand Food Standards Code.

Tree nut allergies are commonly reported to almond, Brazil nut, cashew nut, hazelnut, walnut, pecan nut and pistachio nut; and less commonly to macadamia nut, pine nut, coconut and chestnut (Goetz et al., 2005). Regional variations exist with regards to the specific nut most commonly implicated in severe allergic reactions, probably reflecting local consumption patterns as well as other environmental factors such as exposure to pollen allergens. Cashews were most commonly involved in severe non-fatal food allergic reactions reported in the UK and Ireland during 1998–2000 (Macdougall et al., 2001).

In Norway, hazelnut appears to be the most common trigger of allergic reactions to tree nut (Løvik et al., 2004). A retrospective review of 213 peanut or tree nut allergic children in Australia revealed that anaphylaxis to cashew nut was more common than to peanut (Davoren and Peake, 2005). Australian data on childhood allergies to almond, Brazil nut, cashew, hazelnut, and walnut, found the estimated prevalence for cashew nut to be the highest at 0.33% (Hill et al., 1997).

5.1.2 *Tree nut allergens*

Most of the major allergens identified in tree nuts are seed storage proteins, particularly the 2S albumins and the 7S, 11S and 12S globulins. The 2S albumins are a group of storage proteins present in many dicotyledonous plants. Several major allergens from tree nuts including Brazil nut, walnut, pecan and cashew nuts have been identified as 2S albumins (Pastorello et al., 1998; Tueber et al., 2002; Breiteneder and Radauer, 2004; Robotham et al., 2005; Moreno and Clemente 2008).

The 2S albumins share the conserved disulphide structure common to all members of the prolamin superfamily. However, the IgE-binding sites on these proteins contain hypervariable loop regions that adopt a variety of conformations which may explain the lack of IgE cross-reactivity between the 2S albumins from various plant species (Mills et al., 2004; Barre et al., 2005). Structural homology between the 2S albumin from pecan nut and walnut was observed by Barre et al. (2005) suggests a molecular basis for IgE-binding cross-reactivity between closely related tree nuts.

The 7S and 11S globulins, also known as vicilins and legumins, are the most wide-spread group of seed storage proteins and are present in mono and dicotyledonous plants including nuts and seeds. Recent studies have confirmed the allergenic nature of the 7S globulin of walnut and cashew nut (Mills et al., 2004); as well as in coconut (Benito et al., 2007). The 11S globulins in almond, cashew and hazelnut have been shown to be allergenic (Beyer et al., 2002; Wang et al., 2003; Mills et al., 2004).

The lipid transfer proteins (LTPs) are polypeptides with a molecular weight of approximately 10 kDa that belong to a family of structurally highly conserved proteins. LTPs are recognised as panallergens in a number of plant species including from hazelnut and walnut (Asero et al., 2000). Environmental factors, such as respiratory sensitisation to pollen from the local flora, may influence the relative significance of certain tree nuts. For example, severe hazelnut allergy is linked to sensitisation to LTP and is common in areas without birch pollen, while the milder form of hazelnut allergy in birch-endemic areas is usually due to cross-reactivity with birch pollen (Pastorello et al., 2002; Flinterman et al., 2008).

Anaphylaxis due to macadamia nut ingestion was first reported in Australia (Sutherland et al., 1999). The patient had a history of infantile eczema and seasonal allergic rhinitis but no history of nut allergy. The authors reported that a 17 kDa protein was serologically cross-reactive with hazelnut. Cases of severe reactions to macadamia nut have been reported recently in Europe, possibly due to the increasing consumption (De Knop et al., 2010).

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There have been several reports of allergic and anaphylactic reactions to pine nut but relatively little is published regarding allergenic proteins. IgE-reactive proteins with molecular weights of 17, 50 and 66–68 kDa have been reported (Roux et al., 2003).

Severe and anaphylactic reactions to coconut have been reported (Tueber et al., 1999; Rosado et al., 2002; Roux et al., 2003). However, the literature suggests that reactions to coconut are relatively rare compared with other tree nuts (ASCI, 2010a). A 7S globulin has been identified as an allergen (Benito et al., 2007).

Chestnut is the third most-prevalent food allergen among both adult and paediatric allergy patients in Korea (Lee, 2004). In Asia, Southern Europe and Turkey, chestnuts have been part of the staple diet and a major source of complex carbohydrate for centuries. Chestnut consumption in Australia and New Zealand is limited and allergic reactions to chestnut have not been reported. Two allergens, Cas s 5 and Cas s 8, from chestnut have been described and cloned. Cas s 5 contains an N-terminal domain with homology to the hevein-like domain, the panallergen associated with latex-fruit syndrome. Cas s 8, is a member of another panallergen family, the LTPs (Roux et al., 2003).

5.1.3 *Cross-reactivity among tree nuts*

Serologic cross-reactivity among tree nuts was studied by Goetz et al. (2005). Walnut, pecan, and hazelnut form a group of strongly cross-reactive tree nuts. Hazelnut, cashew, Brazil nut, pistachio, and almond form a group of moderately cross-reactive tree nuts. Cross-reactivity between these groups is less pronounced (notably limited cross-reactivity between walnut or pecan nut and Brazil nut). The strongest cross-reactivities among tree nuts appear to follow botanical family groups; i.e. walnut and pecan in the family *Juglandaceae*; and cashew and pistachio in the family *Anacardiaceae*.

5.1.4 *International regulations*

In Europe, the following tree nuts have been identified as important allergens: almonds, hazelnuts, walnuts, cashews, pecan nuts, Brazil nuts, pistachio nuts, macadamia nut and Queensland nuts. Coconuts, chestnuts and pine nuts are not included on the list.

In Canada, the following tree nuts are included in the list of priority food allergens: almonds, Brazil nuts, cashews, hazelnuts, macadamia nuts, pecans, pine nuts, pistachios and walnuts. Coconut and chestnut are not included on the list.

5.1.5 *Conclusions*

- A significant volume of literature on tree nut allergy has become available since the mid 1990s, when the Australian and New Zealand allergen regulations were being developed. This information more clearly identifies the specific tree nuts involved in the majority of allergic reactions.
- Tree nuts most commonly implicated in allergic reactions are: almonds, Brazil nut, cashew, hazelnut, macadamia nut, pecan nut, walnut, pistachio nut and pine nut. Coconut and chestnut appear to be less frequently associated with tree nut allergy.
- In line with the European and Canadian approach, a list identifying those tree nuts that are most relevant to food allergy in Australia and New Zealand will improve the clarity of the mandatory requirements.

5.1.6 Recommendation

- FSANZ to consult with the Food Allergy and Intolerance Scientific Advisory Group on the development of a list of the tree nuts that are considered important allergens, and consider options for defining the term tree nuts in the context of allergen declaration.

5.2 Collective term: 'fish'

The current list of substances subject to mandatory declaration requirements (clause 4 of Standard 1.2.3 – Mandatory declaration of certain substances in food) includes **fish** and **crustacea**. The term '**fish**' is defined in the Code⁴ to mean aquatic vertebrates and invertebrates including shellfish. Based on this definition, the term **fish** in Standard 1.2.3 is interpreted to include finfish and shellfish (i.e. crustaceans and molluscs). However, Standard 1.2.3 is inconsistent in that it requires crustacea to be declared separately from fish, but does not specify the declaration of molluscs. Also, clause 4 of Standard 1.2.4 sets out the conditions for the use of generic names including '**fish**' requiring crustacea to be declared by their specific name in the list of ingredients, but does not have specific provisions for finfish or molluscs. Consumer and industry stakeholders have raised concerns with FSANZ regarding the inconsistency and lack of clarity in relation to the declaration of molluscs.

The purpose of allergen declaration is to alert allergic consumers to the presence of food or food groups which they need to avoid. The term '**fish**' as defined in the Code includes the three main groups of aquatic animals commonly consumed as food, i.e. finfish, crustacea and molluscs. These three food groups are also collectively referred to as '**seafood**'⁵. In the context of allergen declaration, such generic terms do not provide adequate information to allergic consumers to identify the specific food or food group of concern to them. This is particularly the case for food groups which represent different allergens; i.e., where there are likely to be consumers who need to avoid one food group (such as crustaceans or molluscs), but not another (such as finfish). Therefore, the relevant information to consider is whether finfish, crustaceans and molluscs represent allergenically distinct groups.

Seafood is an important source of human nutrition in many countries around the world. The three main groups in this food category, i.e. finfish, crustacea and molluscs, cause severe allergic reactions, including anaphylaxis. Most information on the prevalence and incidence of severe reactions to seafood is based on studies on patient materials and selected groups (Sampson, 2000; Sicherer et al., 2004; Taylor, 2008). Only a few population-based epidemiological studies are available in the literature. Two such studies from the USA estimated the prevalence of seafood allergy in adults to be between 1.3% and 2.8% (Sicherer et al., 2004; Vierk et al. 2007).

The term 'shellfish' is commonly used to refer to a diverse group of species of crustaceans and/ or molluscs representing the two Phyla – Arthropoda and Mollusca. Crustaceans, a Class within Arthropoda, include prawn, crab, lobster, crayfish and barnacles. The Mollusca Phylum includes abalone, oyster, mussel, scallop, squid and octopus.

⁴ Standard 2.2.3 – Fish and Fish Products: 'in this Code **fish** means any of the cold-blooded aquatic vertebrates and aquatic invertebrates including shellfish, but does not include amphibians and reptiles'.

⁵ Standard 4.2.1 (Australian only standard) – **seafood** means all aquatic vertebrates and aquatic invertebrates intended for human consumption, but excludes amphibians, mammals, reptiles, and aquatic plants.

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Shellfish allergy is an important cause of food induced anaphylaxis around the world for both children and adults (Kandyil and Davis, 2009). Studies from Europe and the USA estimate that shellfish allergy affects around 2% of the population, four times higher than the estimated prevalence of allergy to finfish (Rona et al. 2007, Sicherer et al., 2004, Vierk et al. 2007). Ben-Shoshan et al., 2010) reported that the prevalence of physician-confirmed shellfish allergy to be 0.73% in the Canadian population. In Australia, 5.9% of households participating in an internet survey perceived that at least one family member has shellfish allergy (Allen et al., 2009).

The following is a summary of the scientific and clinical information available on the allergenicity and cross-reactivity of finfish, crustaceans and molluscs.

5.2.1 Allergy to finfish

Allergy to finfish is estimated to affect 0.4% of the USA population (Sicherer et al., 2004; Vierk et al. 2007). A similar estimate was reported in the European population (Rona et al., 2007). In Canada, the prevalence of physician-confirmed fish allergy was reported to be 0.1% (Ben-Shoshan et al., 2010). Based on an internet questionnaire, the prevalence of self-reported perceived allergy to fish in Australia was 2.5% of households surveyed (Allen et al., 2009).

The majority of fish-allergic individuals are sensitised to parvalbumins, a subfamily of closely related 12 kDa calcium-binding proteins present in high amounts in the white muscles of fish and other lower vertebrates. There is a high degree of sequence homology of the parvalbumins in multiple fish species, which probably accounts for most of the clinical cross-reactivity seen in fish allergic patients (Helbling et al., 1999; Poulsen et al., 2001; Swoboda et al., 2002; Van Do, 2005). Up to 50 % of individuals allergic to one species of fish are at risk for reacting to a second species (Sicherer, 2001; Torres Borrego, 2003).

Parvalbumin, however, was not involved in a clinical case of cross-reactivity between tuna and marlin reported by Kondo et al. (2006); and species-specific allergens have been reported (Yamada et al., 1999; Rosmilah et al., 2005). Recently published studies suggest that variations in the expression levels of parvalbumin in different fish species may determine their allergenicity (Griesmeier et al., 2009; Kuehn et al., 2010).

The major fish allergen parvalbumin is resistant to boiling and to enzymes of the gastrointestinal tract (Elsayed and Asa, 1971). A number of other fish allergens are temperature sensitive which may explain why cooked or canned fish can be tolerated by some allergic consumers (Yamada et al., 1999). Cross-reactivity between fish and shellfish has not been reported.

5.2.2 Allergy to crustaceans

More than 30,000 species of crustaceans have been identified, but only a few are commonly consumed as food including prawn, lobster, and crab. Crustaceans are reported in the medical literature to be the most common seafood allergen (Lopata and Jeebhay, 2001; Zhang et al., 2006). In a multi-centre study of the causes of food-induced anaphylaxis in Italian adults, the second most common anaphylactic episodes occurred in patients sensitised to shrimp.

The major allergen in crustaceans has been identified as the 34 kDa muscle protein tropomyosin (Daul et al., 1991; Shanti et al., 1993; Leung et al., 1994; Motoyama et al., 2007). Tropomyosin sequence homology and serological cross reactivity between crustaceans has been reported (Leung et al., 1998a; Leung et al., 1998b; Leung and Chu, 1998).

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Cross-reactivity between a number of crustacean species including prawn, lobster, crayfish and crab is documented (Ayuso et al., 2002, Zhang et al., 2006). Evidence suggests that allergy to one species of crustacean presents a 75% risk of allergic reaction to another species (Sicherer, 2001; Torres-Borrego, 2003).

Closely related tropomyosins have also been identified in molluscs (Miyazawa et al., 1996; Ishikawa et al., 1998). Interestingly, tropomyosin has also been identified as an important allergen in other invertebrates including dust mites and cockroaches. Many shellfish-allergic children have sensitivity to dust mite and cockroach allergens (Ayuso et al., 2002; Kandyil, 2009).

In addition to tropomyosin, two new shrimp proteins, arginine kinase and myosin light chain were recognised by IgE in serum from shrimp-allergic individuals (Yu et al., 2003; García-Orozco et al., 2007; Ayuso et al., 2008). More recently, Ayuso et al., (2009; 2010) identified a sarcoplasmic calcium-binding protein which appears to be of particular importance in the paediatric population.

5.2.3 Allergy to molluscs

The Phylum Mollusca is classified into eight Classes, of which 3 are important as food. These are: Gastropods, e.g. abalone, land and marine snails; Bivalves, e.g. oyster, mussel, scallop, clam; and Cephalopods, e.g. squid, octopus, cuttlefish.

While shellfish allergy is well documented in the medical literature, it is often difficult to ascertain whether molluscs and/or crustaceans are involved. A few cases of allergic reactions to molluscs have been reported from clinics in European countries and Japan (EFSA, 2006; Taylor 2008). Reactions, including anaphylaxis, were reported to abalone, limpet, clam, cockle, oyster, mussel, scallop, snail, squid and cuttlefish (Thong et al., 2005; González Galán et al., 2002; Pastorello et al., 2001; EFSA, 2006; Taylor 2008).

The protein tropomyosin has been identified as the major allergen in many molluscan species (Miyazawa et al., 1996; Leung et al., 1996; Chu et al., 2000; Leung and Chu., 2001). *In vitro* cross-reactivity with IgE antibodies from patient sera have been reported (Leung and Chu, 1998; Leung et al., 1996; Motoyama et al., 2006; Reese et al., 1999). Within the entire mollusc group, tropomyosin sequence identity is between 68% to 100% (Taylor, 2008). Clinical cross-reactivities between molluscan species have been reported, but appear to be fairly uncommon.

As noted in the previous section, tropomyosin is also the major allergen in crustaceans. Tropomyosin from crustacean species and molluscan species share protein sequence identity of 56-68% (Taylor, 2008). Tropomyosin sequence homology is believed to be responsible for clinical cross reactivity between crustaceans and molluscs, as well as non-food allergens such as dust mites (Lopata et al., 2010).

In addition to tropomyosin, a number of proteins have also been identified as putative allergens in molluscs (Taylor, 2008). However, the role of these proteins in allergy to molluscs, possibly as species-specific allergens, is not fully understood.

5.2.4 Conclusions

- Finfish, crustaceans and molluscs are taxonomically distinct groups widely consumed around the world. Clinical allergic reactions to finfish, crustacean and molluscan species have been reported from a number of countries, mainly in Europe, North America and South Asia.

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- The major allergenic proteins in finfish been identified as parvalbumin. Clinical cross-reactivity to multiple fish, in individuals with fish allergy based on the major fish allergen parvalbumin, is commonly observed.
- The major allergenic protein in crustaceans and molluscs is tropomyosin. There is no cross-reactivity between finfish and either molluscs or crustaceans; i.e. individuals with allergy to finfish only, are able to consume molluscs and crustaceans and *vice versa*. Tropomyosin sequence homologies are found in the commonly edible crustaceans and molluscs, however evidence of clinical cross-reactivity between these two groups is limited.
- Molluscs and crustaceans are allergenically distinct from finfish. Therefore, the terms **'fish'** and **'seafood'** as defined in the Code, are not useful in the context of allergy to finfish, crustaceans and molluscs. Terms that allow consumers to identify the specific group would be more compatible with the intent and purpose of allergen declaration requirements.

5.2.5 Recommendation

- FSANZ to consider this issue further in consultation with the relevant stakeholders in Australia and New Zealand. In particular, information from the food industry and food service sector in relation to current practices and commonly used terms, would assist in developing options to improve the clarity of the mandatory declaration requirements.

5.3 Gluten containing cereals

Gluten containing cereals are subject to the mandatory declaration requirements in Standard 1.2.3 of the Code. The specified cereals (i.e. wheat, barley, oats, spelt and their hybridised strains) and their products must be declared when present in food. The requirements address two distinct types of immunologically mediated adverse reactions caused by dietary intake of cereals, i.e. coeliac disease, and immunoglobulin (Ig) E-mediated food allergy. The pathogenic mechanisms underlying these types of adverse reactions are different.

Stakeholder submissions to FSANZ highlighted the difficulty in interpreting the Standard in the context of the two different adverse reactions to gluten-containing cereals. For example, the stakeholders indicated that it is not clear whether all wheat ingredients must be declared if an ingredient has no detectable gluten but is derived from wheat. Also, some stakeholders are concerned that triticale grain, which is a hybrid of wheat and rye, is used in products labelled as 'wheat free', even though triticale is covered by the current declaration requirements in Standard 1.2.3. The stakeholders suggest it may be clearer to food manufacturers if triticale was specifically listed along with other cereals containing gluten.

5.3.1 Gluten

The term 'gluten' refers to the rubbery mass that remains when wheat dough is washed to remove starch granules and water-soluble constituents. Gluten also generically refers to the protein fraction from cereals known to trigger coeliac disease. The cereals are wheat (including spelt and kamut), barley, rye, cross-bred hybrids (e.g. triticale), and possibly oats. Gluten can be separated into gliadin and glutenin proteins according to their solubility in aqueous alcohol.

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The soluble gliadin is a heterogenous mixture of single-chained polypeptides with molecular weights of around 28–55 kDa that can be classified according to their different primary structures into: α -, β -, γ -, and ω -gliadins. The glutenin fraction comprises aggregated proteins linked by interchain disulphide bonds. After reduction of disulphide bonds, the resulting glutenin subunits show solubility in aqueous alcohols similar to gliadins (Bietz et al., 1977; Shewry et al., 2002).

The predominant protein type is low molecular weight (LMW) glutenin subunits; while the high molecular weight (HMW) glutenin subunits are minor components (Wieser, 2007). Prolamins, the alcohol soluble fractions of storage proteins found in wheat, barley and rye, are known as gliadins, hordeins and secalins, respectively. The prolamins of these closely related cereals have a higher composition of proline and glutamine than oats and other distantly related cereals. The glutamine-rich peptide sequences in prolamins of wheat, barley and rye appear to be responsible for their toxicity in coeliac disease (Fraser and Ciclitira, 2001).

5.3.2 Coeliac disease

Coeliac disease (CD) is an immune-mediated gastrointestinal disease triggered by the ingestion of gluten in genetically susceptible persons. The abnormal immune response is characterised by an inflammatory reaction in the small intestine leading to flattening of the mucosa. As a result, affected individuals absorb food and nutrients poorly. This can result in bowel symptoms and deficiencies of vitamins, minerals and other nutrients. CD has several autoimmune features, including the production of highly disease-specific IgA and IgG autoantibodies when patients are on a gluten containing diet (Kaukinen et al., 2010).

Tissue transglutaminase (tTG) appears to be an important component of the disease, both as a deamidating enzyme that can enhance the immunostimulatory effect of gluten and as a target autoantigen in the immune response. Clinical manifestations of CD are commonly associated with various skin and mucosal disorders. Most common and typical among them is dermatitis herpetiformis, which is characterised by skin lesions that may affect several body areas. Comorbidity between CD and other autoimmune disorders has been established. Failure to diagnose and manage CD can lead to serious complications including osteoporosis and malignancy (Fraser and Ciclitira, 2001; Fasano, 2006; West, 2004; Anderson et al., 2007; Barton and Murray, 2008).

The gliadin fraction of cereal protein has been demonstrated to trigger CD with symptoms including mucosal flattening. Although all gliadins are toxic to coeliac patients, the most severe effects are caused by α -gliadins (Ensari et al., 1998; Fraser and Ciclitira, 2001; Hischenhuber et al., 2006).

CD is now recognised as a significant health issue worldwide. Currently, the only effective treatment for CD is a life-long strict avoidance of dietary gluten (Rodrigo-Sáez, 2006; Faulkner-Hogg et al., 2009; Cummins and Roberts-Thomson, 2009; Kaukinen et al., 2010).

Although strict dietary avoidance of gluten is recommended to CD patients, it is probably impossible to maintain. Many food products on the market may contain trace amounts of gluten due to cross contamination (Storsrud et al., 2003). A safe threshold for gluten has recently been under investigation. Based on several studies, a daily intake of 10–20 mg gluten appears to be harmless, whereas daily gluten intake over 200–500 mg is likely to induce small bowel villous damage and inflammation (Hischenhuber et al., 2006; Catassi et al., 2007; Akobeng and Thomas, 2008).

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Oats are genetically different from wheat, rye and barley, and the prolamine content in oats is lower than that of other cereals (Shewry and Halford, 2002). Despite evidence that oats are well-tolerated by the majority of patients with coeliac disease, the inclusion of oats in the diet for CD patients is still a matter of debate (Selby et al, 1999; Arentz-Hansen et al., 2004; Haboubi et al., 2006; Kaukinen et al., 2010). Gluten contamination in commercially available oats has been reported (Thompson 2004; Storsrud et al., 2003).

5.3.3 Allergy to wheat and other cereals

Wheat is the dominant cereal crop in temperate countries and is one of the most commonly consumed cereal crops in many parts of the world (Shewry, 2009). Wheat proteins can be classified into: water-soluble albumins, salt-soluble globulins, ethanol-soluble prolamins, which include gliadins and acid-soluble glutenins. The gliadins and glutenins form the gluten fraction (discussed above).

Both respiratory and food allergies to wheat have been reported in the medical literature. However, reports of food allergy to wheat and related cereals, are relatively infrequent considering the vast dietary exposure.

Wheat allergy develops most commonly in infants, affecting up to 1%, but it tends to disappear within five years (Poole et al., 2006). The main symptoms in children are hives and atopic dermatitis (AD). Occasionally delayed reactions occur after the food is eaten regularly over several days, resulting in eczema or sometimes diarrhoea, or poor weight gain (Hischenhuber et al., 2006; ASCIA, 2010b). Wheat allergy among adults is infrequent, however, reported manifestations include food-dependent exercise-induced anaphylaxis (FDEIA), angioedema and irritable bowel syndrome (Simonato et al., 2001; Morita et al., 2003; Hischenhuber et al., 2006). FDEIA is a rare but well-defined syndrome where the ingestion of food followed by physical exercise can result in an anaphylactic reaction. Anaphylaxis does not occur if exercise is delayed by several hours.

The allergenicity of cereal proteins was initially recognised for its role in the occupational respiratory disease known as bakers' asthma. A number of proteins in the water/salt-soluble fraction (albumins and globulins) have been identified as major allergens associated with the condition (Sanchez-Monge et al., 1992; Baur and Posch, 1998; Amano et al., 1998). In particular, the role of α -amylase inhibitors is considered important but other wheat proteins have been shown to bind IgE from patients with bakers' asthma, including gliadin (Constantin et al., 2008; Bittner et al., 2008). Patients with bakers' asthma reportedly tolerate the ingestion of bread (Armentia, 2009).

A number of studies investigated the profile of allergenic wheat proteins with IgE from patients with various manifestations of wheat allergy (Hischenhuber et al., 2006; Tatham and Shewry, 2008).

Varjonen et al (2000) investigated wheat allergens recognized by IgEs from a group of AD patients suspected of wheat food allergy. Their results suggest that gliadins could be important allergens in this type of allergy to wheat. Palosuo et al. (2001a) studied a group of children with a history suggestive of wheat allergy. Open or double blind oral wheat challenge resulted in immediate symptoms in 48% and delayed symptoms in 20%. The major allergenic protein was identified as the ω -gliadin. IgE antibodies to gliadin were not detected in the children with delayed symptoms.

In a study of 28 children and adults with wheat allergy, confirmed by DBPCFC, Ig E antibodies to various wheat proteins were detected. Seventy two percent showed IgE antibodies against the albumin/globulin protein fraction.

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IgE antibodies against α - and β -gliadins and LMW weight glutenin subunits were detected in 60% of patients, while IgE against lipid transfer proteins (LTP) were detected in 28% of patients (Battais et al., 2003).

In a more extensive study with 60 patients, different antigenic profiles were observed in food allergy to wheat, as a function of age and symptoms (Battais et al., 2005a). Gliadins (α , β and γ) and albumins/globulins appeared to be more important allergens for children with AD with or without asthma, while ω -gliadins were major allergens for adults with WDEIA and/or anaphylaxis (100%), or urticaria (55%).

LMW glutenin subunits also featured in anaphylaxis cases in adults. Only 23% of patients with AD and 8% of those with AD and asthma reacted to ω -gliadins (Battais et al., 2005b).

A study by Daengsuwan et al. (2005) showed that gliadins were also the major allergens in children with wheat-induced anaphylaxis. These studies suggest that differences exist between children and adults in the pattern of response to major wheat allergens and in disease outcome.

In recent years, wheat-dependent exercise-induced anaphylaxis (WDEIA) has been increasingly recognised. Several studies clearly established that for wheat this condition is mainly associated with a group of gliadins, called ω 5-gliadins (Morita et al., 2003; Matsuo et al., 2005). A number of other proteins have also been shown to react with IgE from patients with WDEIA, including glutenin subunits, and related proteins from barley and rye but their clinical significance is unknown (reviewed by Tatham and Shewry, 2008). Mechanisms of eliciting anaphylactic symptoms by exercise were postulated by Inomata (2009). One mechanism is the activated tissue transglutaminase increases the allergenicity of the protein and another is the increased absorption of allergens through the gastrointestinal tract.

In relation to the amount of wheat required to trigger reactions in wheat allergic individuals, a review of the clinical studies suggest that the amount is higher than that for coeliac patients (Hischenhuber et al., 2006).

5.3.4 Cross reactivity among cereal food allergens

Information on clinically significant cross-reactivity among cereals in wheat allergic patients is limited. A study of 145 paediatric patients suffering from AD with a positive skin test to one or more cereals was reported (Jones et al., 1995). Only 21% of patients had symptomatic reactivity as determined by DBPCFC performed using up to 10 g of cereal proteins, and 80% of reactions occurred in response to only one cereal grain (76% wheat). Palosuo et al. (2001b) demonstrated that the γ -70 secalin of rye and the γ -3 hordein of barley cross-react with ω 5-gliadin, a major allergen in WDEIA.

5.3.5 Conclusions

- Wheat allergy and coeliac disease are immunologically mediated adverse reactions to dietary gluten. Wheat allergy in children commonly develops during infancy and is usually outgrown by the age of five.
- Wheat allergy is not common in adolescents and adults but is more likely to persist.
- Gluten triggers coeliac disease and also appears to be a major source of allergens in wheat food allergy.

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- It is now widely accepted that small amounts of gluten daily intake of 10–20 mg are tolerated by the majority of coeliac patients. It has also been suggested that most wheat allergic individuals can tolerate the same, or higher, amounts of wheat protein.

5.3.6 Recommendation

- FSANZ to consult with allergy experts on the current state of knowledge in relation to wheat allergy, including cross-reactivity with other cereals, and if necessary, develop options to improve the clarity of the declaration requirements in relation to coeliac and wheat allergic patients.

6 Exemption of ingredients derived from allergenic foods

There is increasing recognition that some food ingredients derived from allergenic sources present negligible risk to the majority of allergic consumers. However, the effect of food processing operations on different allergens in various food matrices is not always predictable. The following discussion highlights some of the issues in this area.

6.1 Impact of food processing on protein allergenicity

Food allergens are generally proteins of molecular weight more than 9 kDa. The sites on the protein which bind IgE antibodies, known as epitopes, may be conformational or linear. As the name suggests conformational epitopes are dependent on the 3-dimensional folding of a protein for IgE-binding. Consequently, conformational epitopes are more likely to be associated with larger proteins (~>25 kDa) because, unlike short polypeptides they can undergo extensive folding. Such epitopes are also readily inactivated by denaturation of the protein. Linear epitopes are determined by the specific sequence of amino acids in a protein and, therefore, remain active even when the protein is unfolded. Linear epitopes may have a particular clinical significance such as correlation with persistent food allergy (Beyer et al., 2003; Chatchatee et al., 2001; Järvinen et al., 2002).

Food is processed using a variety of techniques including mechanical processing, separation, distillation, thermal processing, biochemical treatment, high pressure treatment, electric field treatment and irradiation (Thomas et al., 2007). In general, allergenic proteins are resistant to processes commonly used in food manufacturing with most allergens retaining their allergenicity after treatment by heat and/or proteolysis. The structural characteristics of a protein influence its stability under various processing conditions and potentially its allergenicity. In addition to the intrinsic properties of the protein, the overall composition of the food, and the past processing history may affect the allergenic potential of processed food. Therefore, in complex food matrices, the overall effect of processing on the allergenicity of food proteins cannot always be predicted (Wal, 2003; Mills et al., 2007).

Scientific investigations of the impact of food processing on allergenicity are further challenged by the fact that proteins can lose solubility as a result of food processing or storage. Consequently, information available on the impact of food processing is largely limited to the soluble proteins that can be extracted for serological or clinical studies.

6.1.1 Thermal processing

Thermal processing is widely used in food manufacturing and most commercial food operations include one or more thermal treatment steps. Thermal food processing methods include boiling, steaming, baking, roasting, drying and pasteurisation. These processes use hot surfaces, steam injection, hot air and microwave heating.

The effect of thermal processing may increase or decrease the allergenicity of proteins depending on a number of factors including the temperature, the duration of heat treatment and the type of thermal processing used, e.g., in the presence or absence of water. However, there are no clear rules regarding the consequences of thermal processing on the allergenicity of food proteins in various food matrices (Wal, 2003; Mondoulet et al., 2005; Mills et al., 2009).

Thermal treatment may cause proteins to undergo significant modifications that affect their physical and chemical characteristics. The loss of tertiary structure is typically followed by unfolding causing a loss of secondary structure, cleavage of disulphide bonds, formation of intra-/intermolecular interactions, rearrangement of disulphide bonds and aggregation. Changes in protein structure result in the loss of conformational epitopes and potentially the loss of allergenicity (Davis and Williams, 1998; Hefle, 1999; Davis et al., 2001; Wal, 2003; Mills et al., 2007; Sathe and Sharma, 2009).

One of the main thermally induced chemical modifications of protein is the Maillard reaction. The reaction occurs when amino acids are heated in the presence of reducing sugars resulting in the spontaneous, non-enzymatic, glycation of proteins. Glycation can affect the structural characteristics and physicochemical properties of a protein. The Maillard reaction is believed to aggregate allergenic proteins thus enhancing their allergenicity by increasing the IgE-binding capacity. Novel epitopes can also be introduced, for example, through changes in a protein's resistance to digestion as a consequence of the Maillard reaction. The IgE-binding capacity of roasted peanuts was approximately 90-fold higher than that of raw peanuts of the same cultivars (Maleki et al., 2000a; Hansen et al., 2003; Mills et al., 2007; Mills et al., 2009).

6.1.2 Enzymatic treatment

Biochemical food processing often involves the use of enzymes including proteases, oxidases or transglutaminases (Paschke, 2009). The allergenicity of some food proteins can be reduced by enzymatic treatment. For example, proteolysis of milk followed by further processing such as ultrafiltration, is used to produce hypoallergenic infant formulas. Hypoallergenic wheat flour can be produced by using bromelain enzyme to cleave the wheat glutenin IgE-binding epitope (Wichers, 2007; Mills et al., 2009). However, enzyme-mediated proteolysis did not destroy the IgE-reactivity of the major peanut allergen Ara h 1 (Maleki et al., 2000b). Therefore, knowledge of the protein structure and the sequence of the IgE epitope, can provide powerful tools to use targeted processes to reduce protein allergenicity.

6.1.3 Physical/ chemical separation of proteins

Processing operations that physically or chemically separate and remove proteins from food, such as distillation, filtration and solvent extraction can reduce the allergenicity of some food ingredients. Specific examples of ingredients derived using physical separation processes are discussed below.

Distillates

Distillation is one of the oldest methods of separating and purifying substances. Distillation is used to separate liquids from nonvolatile substances, or to separate two or more liquids that have different boiling points.

Distillation relies on the difference in the boiling points of the components in the aqueous solution to be separated. The mixture is heated to the boiling point so that components with lower boiling temperature will preferentially vaporise first. The vapour is then cooled to liquefy and the resulting liquid is collected. Initially, low boiling components are collected but as the distillation proceeds, these components are depleted from the starting mixture and higher boiling components begin to distil over. In commercial distillation, the operation is usually well controlled to prevent higher boiling components in the starting material from being carried over to the distilled product.

In the food industry, distillation is commonly used for alcoholic beverages and to purify alcohol for use as a solvent in the formulation of flavours and other food ingredients. Alcohol is produced by fermentation of sugars from various sources, including allergenic foods such as cereal grains and milk whey. Fermentation alone does not eliminate the allergenic proteins present in the mixture, and fermentation products usually contain proteins and protein fragments. The alcohol content is maintained at 12-15% because the fermenting yeast is destroyed at high alcohol concentrations.

Alcohol distillation is used mainly to achieve higher alcohol content but it also removes proteins and other substances present in the fermented product. There is general scientific agreement that non-volatile substances such as sugars (e.g. lactose from whey) and proteins do not distil and therefore, would not be present in the distilled product. The European Food Safety Authority (EFSA) considered a number of analytical studies using total protein and protein-specific detection methods. EFSA concluded that these studies provided supporting evidence that proteins from cereal grains and whey, as well as lactose, were not detectable in distilled products (EFSA, 2007a; EFSA 2007b). Based on these studies, determined that, in a properly controlled process, distillates made from whey and cereals are unlikely to trigger a severe allergic reaction in susceptible individuals (EFSA, 2007a; EFSA, 2007b). Under European Commission legislation, these products are exempt from allergen declaration.

Recently, Cressey et al. (2010) reported on the analysis of distilled ethanol from whey provided by a New Zealand manufacturer. Thirty five samples were analysed for residual protein using Enzyme linked immune-sorbent assay (ELISA) specific for the milk whey protein β -lactoglobulin (β -LG) with a limit of detection (LOD) 2.5 mg/L. No samples contained detectable β -LG. Absence of whey proteins was further confirmed by liquid chromatography-mass spectrometry (LC-MS) analysis.

Distillation products may be processed further to produce foods and ingredients. Down-stream products, such as vinegar derived from distilled alcohol, would not be expected to contain whey proteins. Cressey et al. (2010) analysed seven commercial samples of vinegar produced in New Zealand by secondary fermentation of distilled whey ethanol, for residual whey proteins. Based on ELISA method, no samples contained detectable β -LG at a detection limit of 2.5 ppm (mg/L) and no residues of whey protein were detected by LC-MS.

Glucose derived from cereal grain starch

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Glucose syrups are extremely versatile sweeteners, and are widely used in confectionery products, soft drinks, sports drinks, jams, sauces and ice creams. Wheat starch is commonly used for the commercial manufacture of glucose syrup in Australia.

Wheat starch is also known to contain various proteins, including gluten, the protein involved in coeliac disease and in allergic reactions to wheat. The amount of protein associated with the starch fraction can vary considerably depending on the method of preparation.

Starch granules contain intrinsic proteins embedded in the starch matrix – mainly enzymes involved in starch synthesis (Rahman et al., 1995). In addition, a large number of proteins are associated with the surface of the starch granule (Kasarda et al., 2008). The majority of these proteins were identified as gluten (glutenins and gliadins) and non-gluten (albumins and globulins) proteins. Because starch synthesis occurs in a separate cellular compartment to gluten and other storage proteins, the presence of these proteins in starch is most likely due to the breakdown of organelles during grain maturation. Also identified on the surface of starch granules were proteins which protect the grain from biotic and abiotic stresses (Kasarda et al., 2008).

Glucose is produced by enzymatic hydrolysis of starch. The enzyme alpha-amylase is used for the liquefaction (or thinning) of starch into dextrans, and another enzyme, for example amylogucosidase, is used for the final saccharification resulting in a syrup of high glucose content. The hydrolysis degrades the starch granules releasing the proteins and lipids. Further steps include centrifugation and/ or filtration, physical screening and ion exchange. Cereals such as wheat and barley contain gums which increase the viscosity and reduce the filterability of aqueous extracts of the cereals including glucose syrups.

In 2007, EFSA evaluated data on glucose syrups derived from barley and wheat. EFSA noted that most of the protein is removed during starch manufacturing and that different purification steps, in particular the active carbon treatment, removes proteins and other nitrogen-containing compounds (EFSA, 2007c; 2007d). Residual gluten and peptides were detected by mass spectrometry and liquid chromatography analysis (0.3-1.4 mg/kg) in the final glucose syrup. Gluten levels were below 25.3 mg/kg using a gluten-specific ELISA with (3.1 mg/kg LOD). EFSA considered the analytical and dietary exposure data in the context of the clinical evidence for coeliac disease and wheat allergy, and concluded that it is not very likely that this product will trigger a severe allergic reaction in susceptible individuals. Under European Commission legislation, glucose syrups derived from wheat and barley are exempt from allergen declaration.

Six samples from different runs of wheat glucose syrup manufactured in Australia were analysed using a gluten-specific ELISA method and the Bradford protein assay (Cressey et al., 2010). Gluten was below the LOD, i.e. <3 mg/kg, in three out of six samples; and was 8, 15 and 22 mg/kg in the remaining three samples. Total protein levels detected were 8-16 mg/kg.

Refined oils

Many of the edible oils and fats are derived from the major allergenic foods i.e., soybeans, peanuts, tree nuts and sesame seeds. Crude oils are minimally processed and usually contain various levels of protein from the source food. Martín-Hernández et al. (2008) reported that the protein profile of the cold-pressed soy oil is very similar to that of soy flour. Teuber et al (1997) analysed the protein content in a number of commercially available oils and concluded that oils that underwent least processing at lower temperature had higher protein concentrations.

Crude oil can be further processed to produce refined oil or N/RBD oil. Refining involves a series of steps including degumming, neutralising, bleaching and deodorising. Such highly

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refined oils contain no detectable, or extremely low, protein levels (Taylor and Hefle, 2001; Martín-Hernández et al., 2008).

Although a number of DBPCFC studies showed that highly refined oils do not provoke allergic reactions in susceptible consumers (Taylor et al., 1981; Bush et al., 1985; Hourihane et al., 1997; Crevel et al, 2000), the debate on the safety of these oils for allergic consumers, particularly peanut oil, remains unsettled. Some of the concerns raised relate to the small number and/or insufficient clinical characterisation of allergic individuals tested, the limited number of oils tested compared to the range of products and blends available commercially, and the lack of standardised and validated methodology that can be used routinely for maintaining process specifications (EFSA, 2004b; Hildago and Zamora, 2006; Wilchers, 2007). Recent publications describe improved methodology for the detection of protein in oil (Ramazotti et al., 2008; Jablonski et al., 2010).

Nevertheless, based on more thorough investigations, scientific consensus now exists that refined soybean oil, produced by hot solvent-extraction, bleaching and deodorising, is not likely to cause severe allergic reactions in soy-allergic individuals (Taylor et al., 2004a; EFSA, 2007e).

6.1.4 *Conclusions*

- Food processing can alter the allergenicity of food proteins. The impact of a given process may differ from one allergenic food to another. Proteins may undergo significant physical and chemical modifications as a result of food processing. The intrinsic characteristics of the proteins and the food matrix, as well as the processing method and processing environment affect the outcome. In addition to processes discussed in this report, other processes may be considered on a case-by-case basis, as appropriate.
- Processes that physically or chemically separate food constituents can result in undetectable, or only residual, levels of protein in the processed products. However, reliable and easy to use protein detection methodologies are generally required to ensure process specifications are consistently achieved. Consideration of clinically relevant data is also required to determine the safety of food products derived from allergenic sources.
- A well-controlled distillation operation is probably unique in its ability to eliminate non volatile substances, including proteins, from liquid mixtures.

6.1.5 *Recommendation*

- FSANZ to consider, on a case-by-case basis, the scientific and clinical data available on the impact of food processing on the allergenicity of food ingredients derived from allergenic sources. In consultation with the food industry, FSANZ to develop options to reflect the evidence base through guidance and/or regulatory amendments.

7 Allergen thresholds

An allergen threshold is defined in practical terms as the amount of a specific food that would elicit mild, objective symptoms in highly sensitive individuals. The amount of food capable of eliciting a reaction is variable, possibly over an order of magnitude or more between different individuals, with the same type of food allergy. Many factors contribute to this variability. Intra-individual variability may also occur as a result of extrinsic factors, such

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as exercise, alcohol and concurrent infection. Also the thresholds for different allergenic foods are likely to be different due to differences in the inherent potency of allergens (Taylor et al., 2002).

Where allergenic ingredients are not deliberately added, the reality of food production and processing means that cross-contamination may occur in the supply chain or during food manufacturing. Information on thresholds is critical for developing and maintaining effective allergen control strategies.

7.1 Clinical data

Individual clinical thresholds lie between the No Observed Adverse Effect Level (NOAEL), the highest dose observed not to produce any adverse effect and the Lowest Observed Adverse Effect Level (LOAEL), the lowest dose that is observed to produce an adverse effect (Crevel et al., 2008).

However, the exact point is difficult to determine due to the limitations of dose selection and the sensitivity of clinical measuring techniques. There is also clinical data suggesting that individual thresholds may vary over time. These variables, together with the limitations of human studies, make it unlikely that absolute experimental thresholds for food allergens can be obtained. Because low doses are sometimes used in the diagnosis of food allergies, clinical data could be used to determine the LOAELs for a number of food allergens. Analysis of such data indicates that a wide dose range exists among patients allergic to specific foods. However, the estimation of thresholds from this data was not possible due to the use of different procedure for performing DBPCFC and the lack of NOAEL data (Taylor et al., 2002).

In addition to differences in clinical testing protocols, the data is often based on a few individuals in any one study. There is also the question of whether the patients selected for these studies are representative of the entire population of individuals with allergies to that specific food since most clinics exclude the seriously affected patients (i.e. with a history of anaphylactic shock). Also, a number of factors may affect threshold levels, including exercise, disease, concurrent seasonal allergy and pharmaceutical treatments (Taylor et al., 2009).

A prerequisite to setting thresholds is the systematic collection of clinical food challenge data, using consistent protocols from a representative sample of the full range of food allergic individuals including those at greatest risk. To achieve this, a consensus protocol for clinical studies was developed to facilitate the comparative analysis of data from various sources (Bindsvlev-Jensen et al., 2004; Taylor et al., 2004). A common clinical testing procedure using low doses of various food allergens is critical to facilitating the combined use of data from multiple sources (Crevel et al., 2008). Work is underway in allergy clinics, mainly in Europe, to generate and analyse the data needed to establish individual and public thresholds.

At the population level, the distribution of thresholds from a range of allergic individuals representing the allergic population, can be generated from individual threshold data. Emerging information from statistical modelling studies, using data sets from published older studies and clinical records, on peanut allergy provides an insight into the feasibility of using threshold distribution to establish population thresholds (Taylor et al., 2009; Taylor et al., 2010). The latter study analysed a large clinical dataset (obtained from University Hospital, Nancy, France) where diagnostic peanut challenges had been conducted on all prospective peanut-allergic patients at that clinic using a consistent challenge protocol over a period of more than 10 years. The study confirmed the usefulness of the approach to predict the eliciting doses. This is an important first step in establishing the evidence base to underpin allergen risk assessment and allergen control measures in the food industry.

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Probabilistic modelling is considered to be the most promising approach to allergen risk assessment (Madsen et al., 2009). Probabilistic modelling can be used to estimate the possible impact of inadvertent allergen residues in food products (Spanjersberg, 2010). However, the methodology requires quantitative data on consumption patterns within allergic consumer groups and levels of allergens in food as well as population thresholds. Inevitably, where solid data are not available, assumptions are made which may influence the outcome to various degrees (Spanjersberg et al., 2007; Kruizinga et al., 2008).

While significant progress has been made in the past few years in generating threshold data and in developing allergen risk assessment methodologies, there are still a number of areas that require further investigation. For example, the potential impact of food processing and food matrix on thresholds and on allergen detectability, has been recognised. There is also a need for accurate analytical data on levels of allergens in food that is supported by quality control and reference materials.

Another issue is how to assign numerical values for symptom frequency and severity during clinical testing, and how to incorporate this information into risk modelling (Mills et al., 2010). Ultimately, it needs to be acknowledged that, even through the most rigorous allergen control systems, zero risk is not achievable and, in this context, a community consensus on the acceptable level of risk is needed to effectively minimise precautionary labelling (Madsen et al., 2009; Madsen et al., 2010).

7.1.1 Conclusion

Significant advances have been made in the area of thresholds in the last decade including improved methodologies for gathering and analysing clinical data. Emerging evidence indicates that statistical modelling approaches can be used to establish population threshold levels. This is a critical step to underpin allergen risk assessment and guide allergen control measures in food manufacturing.

7.1.2 Recommendation

In collaboration with the Scientific Advisory Group, FSANZ to maintain a watching brief on scientific developments in the area of allergen thresholds.

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