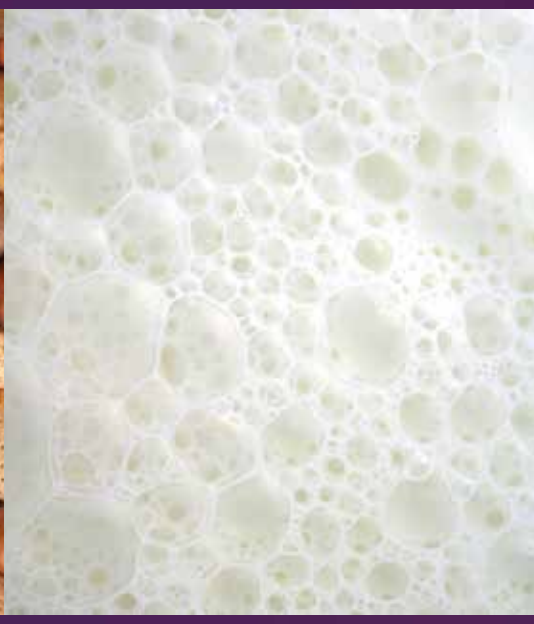
Food Safety
AUTHORITY OF IRELAND

Report of the Scientific Committee
of the Food Safety Authority of Ireland

2019

Information required for the risk assessment of undeclared food allergens in Ireland





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ABBREVIATIONS

CSO
Central Statistics Office

DNA
deoxyribonucleic acid

EC
European Commission

EU
European Union

ED
eliciting dose

EFSA
European Food Safety Authority

ELISA
enzyme-linked immunosorbent assay

et al.
and others (Latin: *et alii*)

FBO
food business operator

FIC
food information to consumers

FSAI
Food Safety Authority of Ireland

GMO
genetically modified organism

HIPE
Hospital In-Patient Enquiry

HSE
Health Service Executive

IFAN
Irish Food Allergy Network

IgE
immunoglobulin E

JRC
Joint Research Centre

LCI
lower confidence interval

N I
Northern Ireland

PCR
polymerase chain reaction

PCRS
Primary Care Reimbursement Service

S.I.
Statutory Instrument

USDA
United States Department of Agriculture

VITAL
Voluntary Incidental Trace Allergen Labelling

1. BACKGROUND

For individuals with a food allergy, avoidance of foods containing the relevant allergen is a key aspect of managing this condition. Some protection is offered to consumers with allergies through EU legislation that requires the declaration of 14 specified allergens[1] when they are used as ingredients in prepacked and non-prepacked foods. The Food Safety Authority of Ireland (FSAI) is responsible for enforcing legislation on food allergen declaration. When a food on the market is discovered to contain any of the 14 allergens which is not declared as an ingredient, remedial action may be required by the relevant food business. The urgency and extent of any remedial action, e.g. relabelling or product withdrawal/recall, can be informed by a risk assessment to be carried out by the food business and/or the FSAI, taken together with other pertinent factors.

2. OBJECTIVE

The goal of this report is to provide scientific advice to the FSAI on the data inputs needed for the risk assessment of undeclared allergens in foods to underpin proportionate risk management in order to protect public health.

3. FOOD ALLERGIES

Many foods can cause a hypersensitive reaction in susceptible consumers who are allergic to, or intolerant of, a particular food or ingredient. The overall prevalence of food allergies in Europe is estimated to be 3% of the European Union (EU) population of approximately 500 million citizens (EFSA, 2014). It is difficult to ascertain the prevalence of the various food allergies in Ireland, as the available data are incomplete and only a proportion of them are based on a medical diagnosis. A study carried out in Ireland on 1,355 children up to two years of age indicated that the overall food allergy prevalence for that age group was 4.5%, with eggs (3%), peanuts (1.8%) and cow's milk (0.7%) being the most common (Kelleher *et al*., 2016). Many children outgrow allergies to milk and eggs, but this is not so common for allergies to peanuts, tree nuts, fish or shellfish. United Kingdom data estimate the prevalence of food allergies in preschool children at between 3% and 6% and in older children and adults at between 1% and 2%, with the prevalence in Ireland likely to be very similar (IFAN, 2018).

Food allergies and intolerances can be associated with a wide variety of symptoms that can occur within minutes or hours following exposure. A typical allergic reaction to food occurs when a person's immune system overreacts via immunoglobulin E (IgE) antibodies (IgE mediated) in response to a specific allergenic constituent (protein) in that food. The more severe allergic reactions (including anaphylaxis) can have potentially life-threatening consequences. Cereals containing gluten are associated with autoimmune (non-IgE mediated) reactions in people with coeliac disease. Sulphur dioxide (SO_2) and sulphites are linked to non-immune-mediated reactions (food intolerance), in which the immune system is generally not involved, and which manifest as metabolic deficiencies (e.g. lactose intolerance) or as pharmacological reactions (e.g. to tyramine).

Food is one of the most common causes of anaphylaxis in Europe, North America, Asia and Australia, with peanuts, tree nuts, milk, eggs, sesame seeds, fish and crustaceans being the foods most commonly implicated (Cianferoni and Muraro, 2012; Huang *et al*., 2012). Peanuts are the most common cause of severe or fatal food-induced anaphylaxis (EFSA, 2014).

A food allergy cannot be cured, but it can be managed by avoiding the offending food(s) or ingredient(s). Therefore, access to accurate food information is essential to enable susceptible consumers to safeguard their own health.

[1] The term 'allergen' in this report refers to the 12 allergens and 2 non-allergens (gluten and sulphites) that are included in Annex II of Regulation (EU) No. 1169/2011 on the provision of food information to consumers.

4. FOOD ALLERGENS ON THE IRISH MARKET

The FSAI has had a food allergen alert system in place since 2009, whereby the reporting or detection of an undeclared allergen in food is rapidly relayed to more than 2,000 subscribed individuals by text and/or email messages. The number of allergen alerts (45) issued by the FSAI in 2018 was the highest since the system was put in place (Figure 1). Allergen alerts can be the result of industry self-reporting (46% in 2016, 53% in 2017 and 64% in 2018), notifications by competent authorities in other EU Member States and third countries (43% in 2016, 33% in 2017 and 27% in 2018), or routine official controls carried out in Ireland (11% in 2016, 13% in 2017 and 9% in 2018). The overall increase in the number of allergen alerts coincides with the rising level of industry self-reporting between 2016 and 2018 and may be related to the FIC Regulation, which came into effect in December 2014, as well as to the greater awareness of food allergens and labelling requirements.

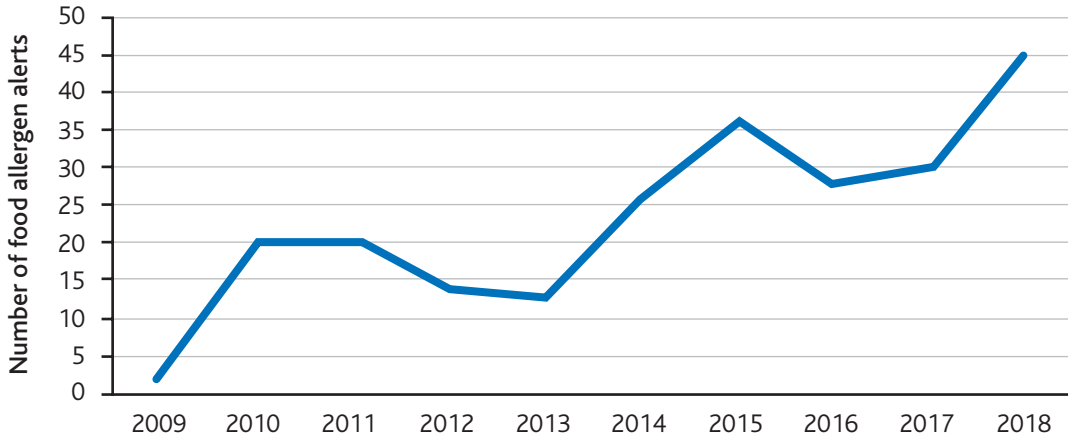

Figure 1 Number of food allergen alerts issued by the FSAI (2009–2018)

Figure 2 shows the breakdown of food allergen alerts issued by the FSAI in 2016, 2017 and 2018 based on the type of food allergen involved. In many cases, a single alert may concern more than one food allergen, and the data demonstrate that the number of alerts involving milk each year is significantly higher than the number of alerts involving the other food allergens.

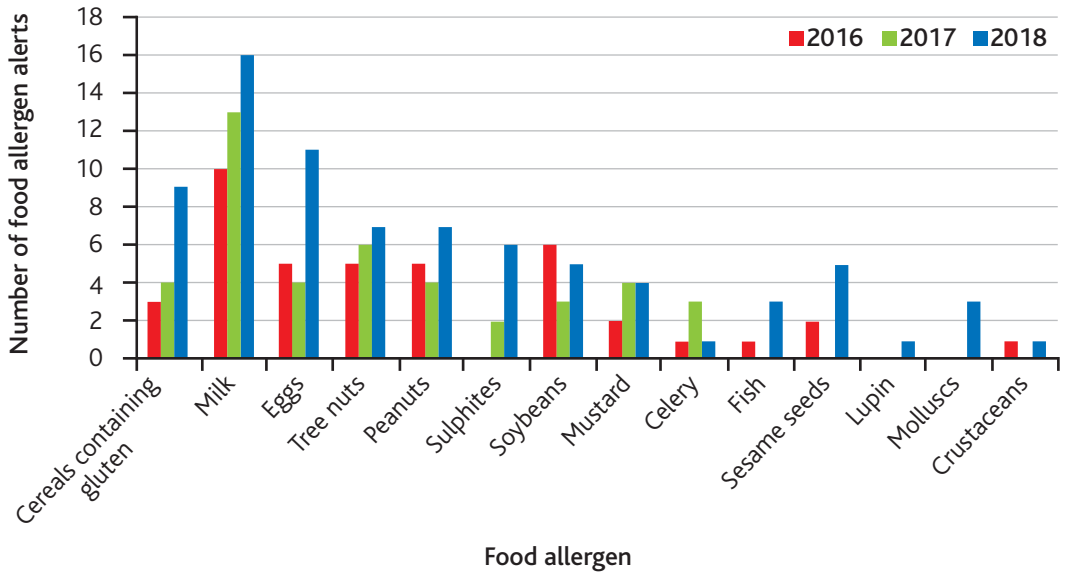

Figure 2 Food allergens associated with FSAI food allergen alerts (2016, 2017 and 2018)

5. EU AND IRISH LEGISLATION GOVERNING THE LABELLING OF FOOD ALLERGENS

Regulation (EU) No 1169/2011 on the provision of food information to consumers (hereafter referred to as the FIC Regulation) (European Union, 2011) mandates that 14 food allergens (Appendix 1) must be declared when they are used to produce food and are still present in the final food. Incorporated into Irish food law by Statutory Instrument (S.I.) No. 556 of 2014 (Government of Ireland, 2014a), the FIC Regulation stipulates that the regulated food allergens must be highlighted or emphasised in the list of ingredients on prepacked foods. The way in which food allergens must be declared for non-prepacked foods varies between EU Member States. In Ireland, such declarations (e.g. "Contains peanuts") must be provided in writing in accordance with S.I. No. 489 of 2014 (Government of Ireland, 2014b).

Cereals containing gluten and sulphites are not considered classic food allergens but are included in the list of 14 regulated food allergens for regulatory clarity and are subject to similar declaration requirements. SO_2 and sulphites must be declared when used and still present in the final food at concentrations of more than 10 mg/kg (10 mg/L) in terms of the total SO_2. This specific labelling threshold provides a sufficient basis for risk management decisions without any further need for risk assessment.

Eight different types of nut are included under the classification "Nuts" in the FIC Regulation, and in this report they are collectively referred to as "tree nuts" in order to differentiate them from peanuts, which are ground nuts. The tree nuts include almond, hazelnut, walnut, cashew, pecan, Brazil nut, pistachio, and macadamia/Queensland nut.

The undeclared presence of food allergens in a food due to cross-contamination may be detected through routine or random checks carried out by regulatory authorities or food businesses, or as a result of complaints. Contaminating food allergens are not considered ingredients intentionally used in the manufacture or preparation of a food and therefore are not subject to the declaration requirements set out in the FIC Regulation. Upon detection of a contaminating food allergen, a risk assessment is required in order to determine whether it constitutes an unsafe food, which cannot be placed on the market in accordance with Article 14 of Regulation (EC) No. 178/2002 (European Commission, 2002). The risk assessment, along with other pertinent considerations, will then help to inform risk managers about the response required (if any) to protect susceptible consumers.

Article 7 of the FIC Regulation stipulates that food information must not be misleading. More specifically, Article 36.2 makes it clear that voluntary food information shall not mislead the consumer, must not be ambiguous or confusing for the consumer and, where appropriate, must be based on relevant scientific data. Voluntary "allergen free" declarations (e.g. "peanut free") indicate to consumers that particular allergens are not present in that food. Foods with such declarations (except for "gluten free") may not contain detectable amounts of those food allergens. Precautionary allergen labels such as "May contain…" are regularly used by the food industry and, when used judiciously, they can be useful for informing susceptible consumers of a risk associated with a particular food. However, these declarations are often used inappropriately and without justification, with the result that their effectiveness for susceptible consumers has been diminished (FSAI, 2012). In accordance with Article 36.3 of the FIC Regulation, a process is being developed at EU level to regulate precautionary allergen labelling.

6. INGREDIENT VERSUS CONTAMINANT

In accordance with Article 9 of the FIC Regulation, the declaration of each of the 14 regulated food allergens is mandatory when they are used in the manufacture of a food and are still present in the final product. In the event of a food on the market being found to contain an undeclared allergenic ingredient, the relevant food business must, in the best interests of consumer safety, address the problem in consultation with the FSAI and relevant official agencies. Mitigation of the risk to susceptible consumers can involve simply adding/amending the allergen declaration or, in more serious circumstances, product withdrawal or even recall. Mandatory food allergen declaration in accordance with the FIC Regulation is not required where a food allergen is present in a food due to cross-contamination. A cross-contaminant is generally viewed as a constituent inadvertently present in a food at relatively low but undefined levels. The undeclared presence of an allergen in a food, even at low levels, can pose a risk to susceptible consumers. The level of risk (if any) posed by the undeclared allergen can be assessed and considered along with other pertinent factors by risk managers to instruct food business operators (FBOs) on how best to mitigate the risk to consumers.

7. RISK ASSESSMENT AND RISK MANAGEMENT

Where an error during production, processing or labelling is identified as the reason that one of the 14 regulated food allergens is not declared as an ingredient in a particular food on the market, remedial action is required by the relevant food business. The urgency and extent of any remedial action can be informed by a risk assessment to be carried out by the food business and/or the FSAI. Where cross-contamination is found to be the cause of the presence of an undeclared allergen in a food, a risk assessment is required in order to inform any risk management actions that may be considered. In Ireland, regulatory risk assessments are carried out by the FSAI. Risk managers at the FSAI, along with the official agencies, take risk assessments along with other pertinent factors into consideration in order to underpin possible risk management actions such as relabelling, product withdrawal (removal from sale) or product recall (request that consumers return the products).

8. RISK ASSESSMENT OF FOOD ALLERGENS

Different approaches have been proposed for the risk assessment of food allergens for labelling purposes (EFSA, 2014). Some probabilistic risk assessment models have also been described (Kruizinga *et al*., 2008; Madsen *et al*., 2009), although the extent of their use in practical situations is unclear.

A risk assessment is carried out in order to inform risk management decisions, which must be effective but proportionate. Established risk assessment models are effective in assessing the potentially widespread risk posed by physical, microbiological and chemical hazards. However, food allergens have the potential to affect only a small proportion of the population, and so a risk assessment must determine not only the level of risk posed by an undeclared food allergen to the subset of susceptible consumers, but also to the population as a whole. Critical factors for the effective assessment of risk to the whole population include the prevalence of the relevant food allergy and the potential exposure to the food containing the allergen. A low prevalence rating and a low potential for exposure would indicate a relatively low risk to the population as a whole, and vice versa. However, where there is a significant risk to the population as a whole, some additional criteria – such as the concentration of the allergen in the food, relevant clinical thresholds and the likelihood of a severe reaction – must also be considered in assessing the risk to susceptible consumers. Therefore, the effective risk assessment of an undeclared food allergen must take into account all possible permutations of the aforementioned relevant factors on a case-by-case basis in order to reach a safe and practical conclusion for the population as a whole, as well as for those susceptible consumers.

9. CRITICAL INFORMATION REQUIRED FOR EFFECTIVE FOOD ALLERGEN RISK ASSESSMENT

Certain information and clarifications are required to enable an effective risk assessment to be conducted, and risk management decisions to be taken, upon receipt of evidence that a food contains an undeclared food allergen:

a) Reliability of the analytical results

b) Prevalence of the individual food allergy in Ireland

c) Potential for a severe reaction

d) Concentration of the allergen in the food

e) Allergenic reaction-eliciting dose (reference dose)

f) Potential exposure to food containing an undeclared food allergen.

9.1 Reliability of the analytical results

The preferred analytical technique for detecting and quantifying food allergens is the enzyme-linked immunosorbent assay (ELISA). However, the use of ELISA for food allergen analysis has a number of limitations, with the result that alternative methods are either in use or in development.

9.1.1 ELISA

ELISA is an analytical technique routinely used to good effect in many laboratory situations. The ELISA method relies on a specific interaction between antibodies produced against certain peptide or protein antigens. It is currently the preferred analytical method of many EU Member States (including Ireland) for official controls, allowing the detection and quantification of food allergens (except sulphites).

A number of factors are known to affect the reliability and reproducibility of ELISA in food allergen detection and quantification. A low antigen concentration in a food can yield a weak positive signal close to the detection/quantification limit, which must be confirmed before a final qualitative or quantitative result can be determined. The type of food matrix and production or processing methods used to manufacture a food can have an impact on the antibody-antigen interactions, which can affect the sensitivity of the ELISA method and thereby result in false negatives or positives, or in inaccurate quantification. In addition, antibody specificity and sensitivity can vary between kit manufacturers, and even between different batches of the same kit. Care must be taken when assessing ELISA results, as antibodies may recognise similar proteins from different allergens (cross-reactivity), resulting in false positives. An example of such cross-reactivity includes antibodies raised to peanut protein which could also recognise antigens on lupin, soybeans, peas, hazelnuts and Brazil nuts (EFSA, 2014).

9.1.2 DNA analysis by polymerase chain reaction

Polymerase chain reaction (PCR) can be used to genetically screen for the potential presence of allergenic constituents in a variety of food matrices. It is a reliable method to detect and identify allergenic constituents because the deoxyribonucleic acid (DNA) molecule is more robust than many proteins and less susceptible to denaturation/degradation by production or processing methods. In addition, the ability to detect and quantify the DNA of an allergenic ingredient at relatively low starting levels is a feature of PCR, while the risk of cross-reactivity can be minimised by appropriate DNA primer selection and sufficiently stringent amplification parameters. However, PCR on its own is not suitable in all scenarios. For example, it is unclear whether current PCR techniques would be able to differentiate between the meat and eggs from a chicken, or between bovine meat and milk. Other possible issues include potential enzyme inhibitors present in some food ingredients that can negatively affect the DNA amplification reaction and result in false negatives or unreliable quantification. If DNA analysis is to be used as a quantitative food allergen detection method, then a reliable conversion factor(s) would be required in order to transform a nucleic acid result into a protein value.

9.1.3 Mass spectrometry

Mass spectrometry is being evaluated for use in food allergen detection and quantification. The method involves extracting protein from a food and digesting it with proteolytic enzymes to yield peptides. The various peptides are separated on the basis of size, either by electrophoresis or liquid chromatography, after which they are ionised and detected using mass spectrometry. The processes of protein extraction and proteolysis, as well as the separation and detection of peptides are all achievable by existing methodologies, although some of these steps can vary in efficiency and thus affect reliability in terms of quantification or reproducibility. However, a significant hurdle to be surmounted is the need for sufficient databases with which to identify individual peptides, and this work is already underway.

9.1.4 Harmonising the analysis of food allergens in the EU

The Joint Research Centre (JRC) is the European Commission (EC) agency charged with establishing and validating analytical techniques and has set up a working panel of EU Member State experts to examine laboratory techniques used to detect and quantify food allergens (European Network of Food Allergen Detection Laboratories). The expert panel will work to harmonise and validate select techniques in the same way that PCR analysis is coordinated for the analysis of genetically modified organisms (GMOs) at EU level. Once this work is complete, EU Member States will then have access to validated analytical techniques which will enable a more harmonised approach across the EU to the detection and quantification of food allergens.

9.2 Prevalence of individual food allergies in Ireland

As previously noted in Section 3, the overall prevalence of food allergies in Europe is estimated to be about 3% of the EU population of approximately 500 million citizens (EFSA, 2014). Turning to the situation in Ireland, in order to estimate the level of risk posed by an undeclared food allergen, reliable data on the number of consumers who are allergic to each of the 14 regulated food allergens are required. For example, an estimated 1% of the population in Ireland has coeliac disease, with up to 6% affected by non-coeliac gluten sensitivity (Coeliac Society of Ireland, 2018).

The gold standard of food allergy diagnosis is an oral food challenge which requires the input of a trained physician. However, where such data are lacking at the large-scale population level, public surveys in their various forms can yield some useful information, although a significant limitation is the difficulty in establishing the veracity of the information received. The FSAI carried out an electronic survey in 2010 in order to determine the prevalence in Ireland of adverse reactions to the consumption of the 14 regulated food allergens. While the survey was open to the public, members of Anaphylaxis Ireland and the Coeliac Society of Ireland were specifically notified. A total of 495 responses were recorded (Figure 3), with 86% of respondents claiming to have been medically diagnosed.

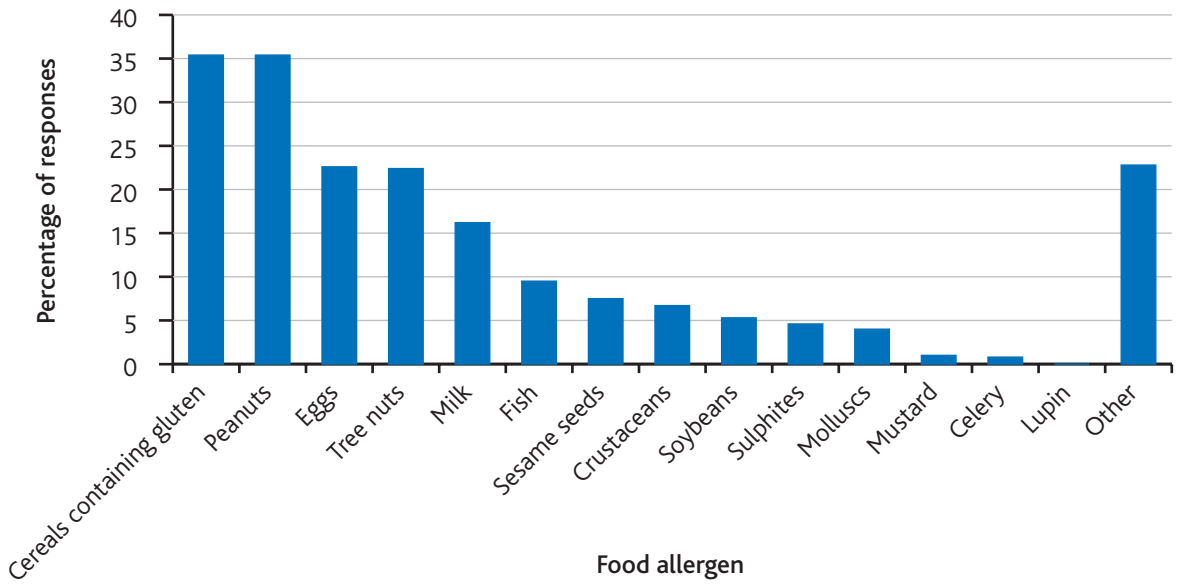

Figure 3 FSAI electronic food allergy survey (2010)

An all-island survey, including both Northern Ireland (N I) and the Republic of Ireland, was conducted in 2013 by *safe*food in conjunction with the Food Standards Agency in Northern Ireland. The goal of this survey was to understand the experiences of members of Allergy N I and Anaphylaxis Ireland when dining out. A total of 241 valid responses were received from the 420 questionnaires disseminated in the Republic of Ireland, with 97% of respondents reporting a medical diagnosis (Figure 4).

Representative bodies for consumers with coeliac disease were not specifically contacted for this survey, with the result that the data relating to cereals containing gluten differ significantly between the 2010 FSAI and 2013 *safe*food surveys. However, the results of both surveys display similar patterns for the other 13 allergens, with the most frequent adverse reactions reported consistently being in response to peanuts, tree nuts and eggs.

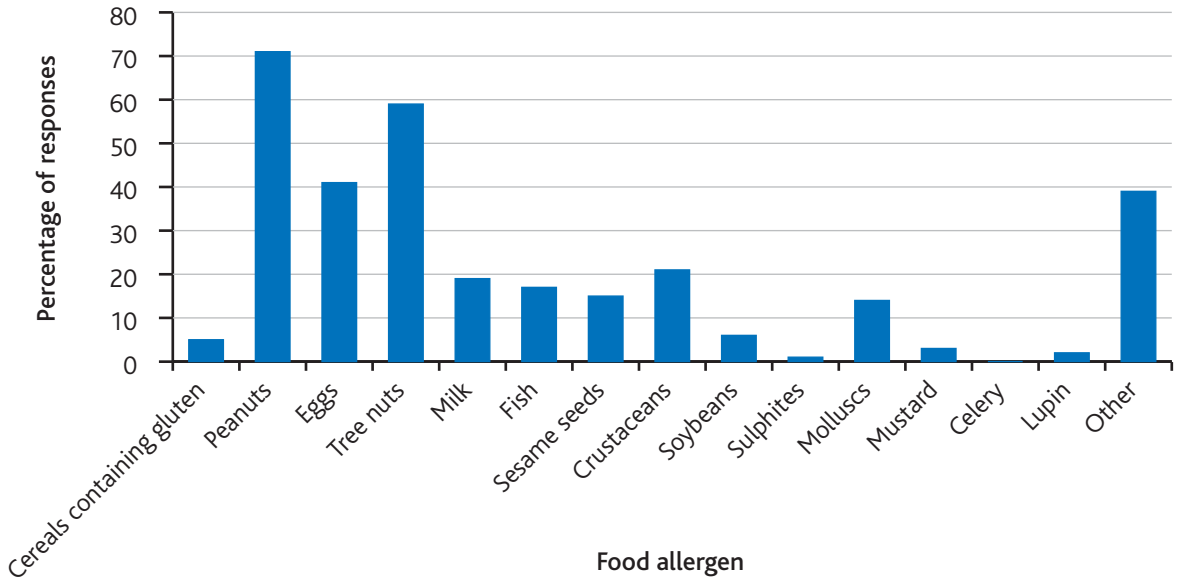

Figure 4 safefood food allergy survey for the Republic of Ireland (2013)

A CensusAtSchool survey questionnaire was completed by 5,348 secondary school students in Ireland between September 2014 and August 2015 (CSO, 2015). The self-reported food allergies identified in decreasing order of frequency were associated with peanuts, cow's milk, eggs, gluten, crustaceans, fish and soybeans (Figure 5).

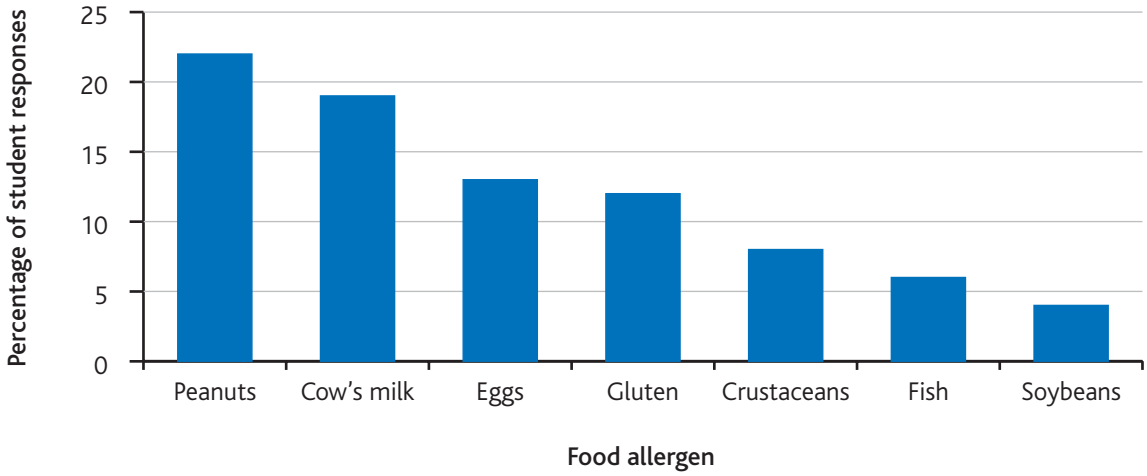

Figure 5 Questionnaire responses from Irish secondary school students (CSO, 2015)

These surveys, along with the 2016 study on young children (Kelleher *et al*., 2016), represent the available data on the prevalence and distribution of food allergies in Ireland at this time, and can be updated once more extensive data become available. While the numbers generated by these surveys may not be an accurate reflection of the actual occurrence of the relevant food allergies in the Irish population, the apparent trends from the different sources are in broad agreement and can be used as an aid for risk assessment purposes. It is important to note that the sensitivity of certain consumers to the different food allergens can be influenced by factors such as the consumer's ethnicity or underlying physical or health issues, as well as by certain types of food processing (Byrne and Hourihane, personal communication, 2019).[2] However, it is not always possible to incorporate all variables into a risk assessment where an undeclared allergen is found in a food product.

9.3 The potential for a severe reaction

Food is one of the most common causes of anaphylaxis in Europe, North America, Asia and Australia, with peanuts, tree nuts, milk, eggs, sesame seeds, fish and crustaceans being the most commonly implicated foods (Cianferoni and Muraro, 2012; Huang *et al*., 2012). Peanuts are the most common cause of severe or fatal food-induced anaphylaxis (EFSA, 2014).

Data from the Irish Hospital In-Patient Enquiry (HIPE 1) database recorded the number of hospital admissions each year over a 10-year period from 1995 to 2004 that were associated with food-related anaphylaxis, with peanuts being the most prevalent cause and, to a reduced extent, fish, eggs and tree nuts (Figure 6). These data have not been available since 2004 and therefore may no longer be a true representation of the evolving Irish population, with strong concerns also expressed by some clinical experts about their reliability. However, more recent HIPE data (HIPE 2) for 2008–2017 provide a general indication of the number of hospitalisations in Ireland due to food-related anaphylaxis (Figure 7).

[2] A Byrne (Consultant Paediatric Allergist, Our Lady's Children's Hospital, Crumlin, Dublin); JO'B Hourihane (Consultant Paediatric Allergist, Cork University Hospital).

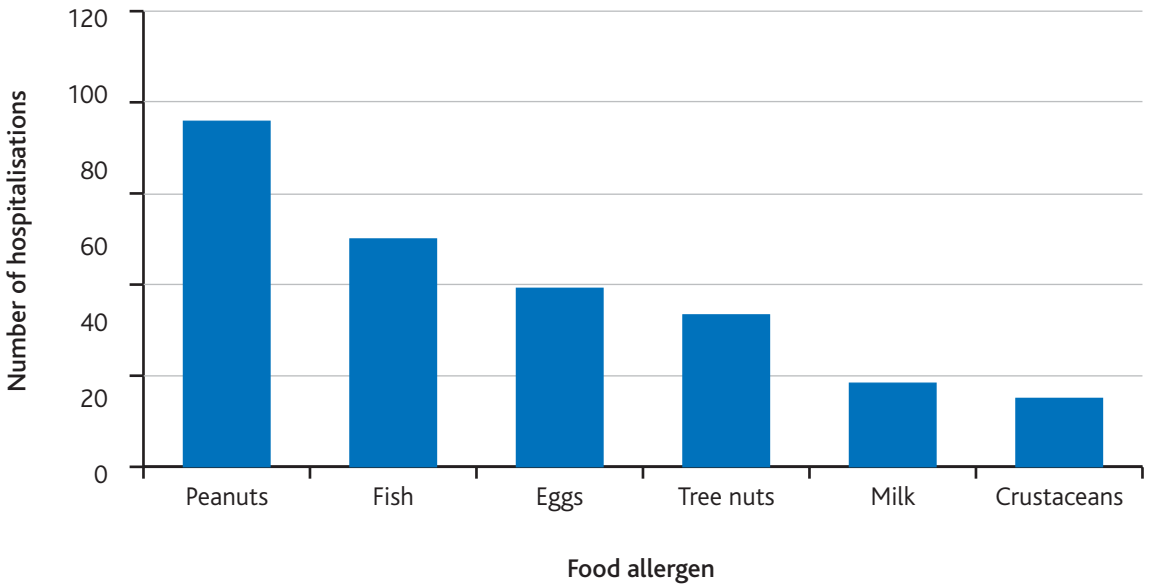

Figure 6 Number of hospitalisations in Ireland due to food-related anaphylaxis (1995–2004)

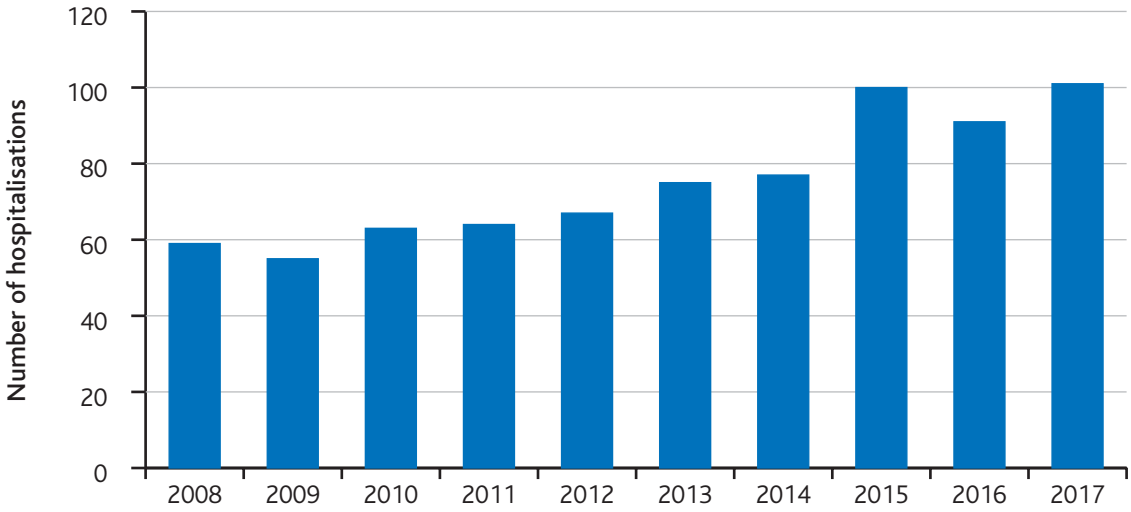

Figure 7 Number of hospitalisations in Ireland due to food-related anaphylaxis (2008–2017)

The European Anaphylaxis Registry collected data (July 2007 to March 2015) on 1,970 children susceptible to anaphylaxis from 90 study centres in 10 European countries, including Ireland. The study (Grabenhenrich *et al*., 2016) concluded that in the first decade of life, food is the dominant elicitor of anaphylaxis compared to insect venom or drug-related anaphylaxis. In children up to two years of age, cow's milk and hen's eggs were the most prevalent elicitors, changing to hazelnuts and cashews in preschool children, while peanuts were a prevalent elicitor in both age groups. The data relating to nine of the 14 regulated food allergens derived from that study (Figure 8) demonstrate that the prevalence of the different food allergies varies between age groups.

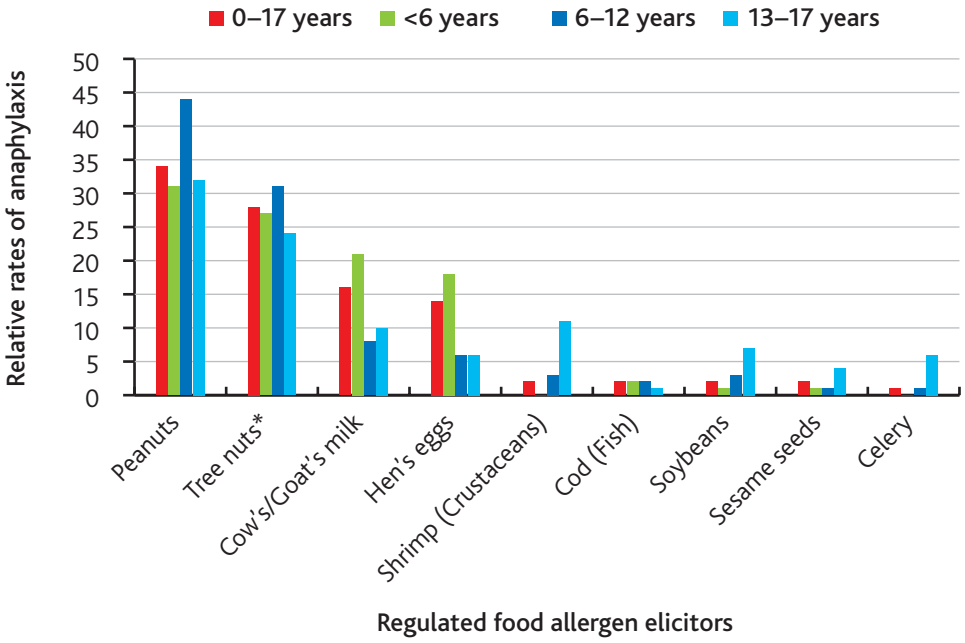

Figure 8 Relative rates of anaphylaxis associated with some of the regulated food allergens in susceptible children up to 17 years of age (derived from Grabenhenrich *et al.*, 2016)

*Includes the eight regulated tree nuts

Epinephrine (also known as adrenaline) is the medication prescribed to people at risk of anaphylaxis, and data provided directly by the Health Service Executive (HSE) Primary Care Reimbursement Service (PCRS) indicate that between January and November of 2017 there were 14,294 individuals in Ireland who had been prescribed pre-filled adrenaline auto-injector devices. The available PCRS data do not discriminate between people with food allergies compared to other allergenic triggers, such as insect venom or drugs; however, clinical experience shows that people with allergies to drugs, and young people under the age of 16 with insect venom allergies, are not generally prescribed these devices (Byrne and Hourihane, personal communication 2019).[3] Food is considered to be the most frequent cause of anaphylaxis in Europe, accounting for between 30% and 50% of anaphylaxis cases in North America, Europe, Asia and Australia, and for up to 81% of anaphylaxis cases in children (Cianferoni and Muraro, 2012). Therefore, it is reasonable to assume that a significant majority of the 14,294 individuals prescribed an adrenaline auto-injector device in Ireland in 2017 were people with severe food allergies.

9.4 Concentration of the allergen and reaction-eliciting dose

A number of EU and international projects have investigated the amount of a particular food allergen required to elicit an adverse response in sensitive individuals, commonly referred to as the eliciting dose (ED). The Voluntary Incidental Trace Allergen Labelling (VITAL) Program is an Australian-based standardised allergen risk assessment tool developed by and for the food industry. It is designed to provide a scientific basis for food businesses to inform consumers of the possible inadvertent presence of a food allergen using precautionary allergen labelling (e.g. "May contain…"). The scientific panel of experts involved with VITAL developed the 'reference dose' concept, which represents the total amount of protein in milligrams from an allergenic food at which only the most sensitive individuals in the population are likely to experience an adverse, though not necessarily a severe, reaction. Where sufficient data are available, it is possible to calculate an ED_{01} with statistical confidence. This is the reference dose at which only 1% of the susceptible population would be predicted to react. However, where the data are insufficient to allow robust calculation of the ED_{01}, the achievable reference dose may only be, for example, the ED_{05}.

[3] A Byrne (Consultant Paediatric Allergist, Our Lady's Children's Hospital, Crumlin, Dublin); JO'B Hourihane (Consultant Paediatric Allergist, Cork University Hospital).

In a recent review (Taylor *et al*., 2018), the reference doses for a number of food allergens were calculated from the published literature (Table 1) based on: (i) the ED_{01} for peanuts and milk; (ii) the 95% lower confidence interval (LCI) of the ED_{05} for soybeans, sesame seeds, lupin, mustard and shrimp (crustaceans); or (iii) both, where the amount of data was borderline for estimation of the ED_{01} (eggs and hazelnuts). The data for hazelnuts available for this review were considered superior to those for cashews, so hazelnuts were selected for the purposes of this report (Table 1) to represent the reference doses for the eight regulated tree nuts until more extensive data become available. The scientific review provides data on shrimp, which for the purposes of this report are considered representative of the reference dose for crustaceans until data on other crustaceans become available. Reference dose values were not provided for fish or celery (celeriac) in the 2018 review, so for the purposes of this report, they were derived from alternative sources as indicated in Table 1. Similarly, for the purposes of this report, a reference dose was calculated for gluten based on published data (Collin *et al*., 2004). However, risk assessments concerning the undeclared presence of cereals containing gluten must be cognisant of the EU labelling thresholds of ≤20 ppm or ≤100 ppm associated with voluntary declarations of "Gluten free" or "Very low gluten", respectively, in line with Commission Implementing Regulation (EU) No 828/2014 (European Union, 2014).

Table 1 Reference doses for 13 of the regulated food allergens (derived from Taylor et al., 2018, unless otherwise indicated)

Allergen	Reference dose[a] (mg protein)	Quantitative risk
Peanuts	0.2	ED_{01}
Tree nuts (hazelnuts)	0.1[b]	ED_{01} and 95% LCI ED_{05}
Eggs	0.03	ED_{01} and 95% LCI ED_{05}
Crustaceans (shrimp)	10[c]	95% LCI ED_{05}
Milk	0.1	ED_{01}
Soybeans	1	95% LCI ED_{05}
Fish (cod)	1.11[d]	MED[h]
Celery (celeriac)	10.5[e]	–
Lupin	4	95% LCI ED_{05}
Sesame seeds	0.2	95% LCI ED_{05}
Mustard	0.05	95% LCI ED_{05}
Cereals containing gluten	30[f]	–
Molluscs	–[g]	–

[a] Reference dose refers to the total protein in milligrams from an allergenic food below which only the most sensitive individuals in the allergic population are likely to experience an adverse reaction

[b] Based on the reference dose for hazelnuts – the most reliable data available for any of the eight tree nuts

[c] Based on the reference dose for shrimp – the only reliable data available for crustaceans

[d] Data corresponding to the minimum (observed) ED of digested cod fish protein extract (EFSA, 2014)

[e] Data calculated from Ballmer-Weber *et al*. (2000), assuming a protein content of 1.5% in raw celery root (celeriac) (USDA National Nutrient Database, 2018)

[f] Cereals containing gluten – the reference dose is 30 mg of gluten based on published data (Collin *et al*., 2004)

[g] Insufficient data available

[h] MED = minimum eliciting dose – exposure levels to codfish below which an allergic individual is unlikely to react.

An EU-funded study on the prevalence, cost and basis of food allergies across Europe (EuroPrevall) set out to deliver the information and tools necessary for policy-makers, regulators and the food industry to effectively manage food allergies across Europe. It aimed to establish the threshold levels for five major food allergens, namely, peanuts, hazelnuts, celery (celeriac), fish and shrimp. The project also set about estimating the ED_{10} (the dose that would elicit a response in 10% of the allergic population). The resulting data supported the view that ED_{05} or ED_{01} values are more appropriate to use for risk assessment purposes, since they offered a greater level of protection for allergic consumers. However, the full results of this work are yet to be published.

9.5 Potential exposure to food containing an undeclared food allergen

The potential exposure of susceptible consumers to a food containing an undeclared food allergen can only be assessed on a case-by-case basis as food incidents arise. Information on the food category within which the allergen is inadvertently present is crucial to identifying a possible increased risk to a particular subpopulation. For example, the prevalence of egg allergies is generally higher in children under three years of age compared with older children or adults (1.5%–2.5% compared with 0.1%–1.0%, respectively; EFSA, 2014), which means that undeclared egg could pose a greater risk in foods targeting young children relative to foods for older children or adults. Additionally, an undeclared food allergen present in a niche product (e.g. a food supplement) would be expected to pose a lower risk of exposure to the overall population compared with a food with wider appeal, such as a bakery or dairy product. Data from food consumption surveys of the general population or of specific population subgroups (e.g. children, adolescents, the elderly) are available in most European countries. However, these surveys were not designed to specifically address the question of food allergies (EFSA, 2014). In addition, food composition tables ignore the distribution of specific allergens present by cross-contamination in the general food supply, which is not known at present (Crevel *et al*., 2014).

Estimates of exposure for risk assessment of food allergens are generally based on acute exposure, i.e. intake of the allergen at a single eating occasion. For a food with a known concentration of an allergen, exposure to the allergen may be estimated as allergen concentration multiplied by portion size, where a large portion size is assumed for a conservative estimate of exposure. In Ireland, data are available on portion sizes of a wide range of foods consumed by children and adults as recorded in the Irish Universities Nutrition Alliance national food consumption surveys (Lyons and Giltinan, 2013; Lyons *et al*., 2013).

10. CONCLUSIONS

The primary function of this report is to provide scientific information to the FSAI which, with a case-by-case exposure assessment, would form the basis of a risk assessment in the event of an undeclared food allergen being detected in a food consumed or destined for consumption in Ireland. In terms of answering the questions asked, the Scientific Committee can conclude the following:

1. ***What is the prevalence of all 14 food allergies in Ireland?***

   The available data for Ireland on the prevalence of food allergies associated with the 14 regulated food allergens is limited to surveys carried out by the FSAI, *safe*food, the Central Statistics Office (CSO) and a 2016 study on young children (Kelleher *et al*., 2016). Coeliac disease is acknowledged to affect approximately 1% of the Irish population and the data available from the aforementioned sources indicate that peanut allergy is the most prevalent of the IgE-mediated food allergies. The remaining IgE-mediated allergies are predominantly associated with tree nuts, milk and eggs, while allergies to lupin, celery and mustard do not appear to be very common in Ireland.

2. ***What are the minimum levels of each of the 12 food allergens that can trigger an adverse response in humans (eliciting doses)?***

A 2018 review of relevant data (Taylor *et al*., 2018) provides the most up-to-date information on the reference doses for many of the regulated food allergens (Table 1). Alternative data sources were used to determine meaningful reference doses for celery (celeriac), fish and gluten, which were not included in the review.

3. ***Analytical capacity for food allergen detection and quantification in the Public Analyst Laboratory is limited, which means that only some of the 14 allergens are sampled for analysis each year. In view of the information to be obtained in points 1 and 2, which of the 14 food allergens pose the greatest risk for Ireland?***

The available data do not facilitate a ranking of the relative risk posed to the Irish population by the 14 regulated food allergens. While the likelihood of reaction to some of the regulated food allergens can vary with age, peanuts appear to pose the greatest food allergy risk to the Irish population in terms of likelihood of, and potential for, severe reaction. The same criteria of prevalence and risk of severe reaction combined indicate that allergies to eggs, milk and tree nuts pose a lower but still significant level of risk, followed by fish, crustaceans and sesame seeds. However, these risk levels may be subject to change in the future in response to evolving infant feeding and weaning recommendations, a changing demographic, an increasingly globalised food supply, evolving food production and processing methods, and ongoing clinical desensitisation trials.

4. ***In view of the information to be obtained in points 1, 2 and 3, what is the maximum level of undeclared allergen (of the 12 without specified thresholds) that would ensure a high level of protection for vulnerable consumers?***

The available information does not allow for a definitive ranking of the risks posed to the Irish population by the undeclared presence of each of the 14 regulated food allergens in food. Therefore, the best assessment of such risks can only be made on a case-by-case basis using the incident-specific exposure assessment along with available data on eliciting doses (Table 1), food allergy prevalence in Ireland and the risk of severe reaction posed by a particular allergen.

11. RECOMMENDATIONS

An effective assessment of the risk to the Irish population posed by the undeclared presence of regulated food allergens is highly dependent on the availability of reliable data. To ensure that sufficient information is available to facilitate effective risk assessments in order to protect public health, the FSAI should:

- Promote areas of research that would facilitate the capture of contemporary data for Ireland in relation to the prevalence of allergies associated with the 14 regulated food allergens and the incidence of severe reactions to those food allergens
- Maintain a watching brief on international efforts to establish and improve threshold data (eliciting doses) and any emerging issues related to food allergies
- Continue to support participation in ongoing efforts at EU level to develop and harmonise food allergen analytical methodologies.

12. REFERENCES

Ballmer-Weber BK, Vieths S, Lüttkopf D, Heuschmann P and Wüthrich B (2000) Celery allergy confirmed by double-blind, placebo-controlled food challenge: A clinical study in 32 subjects with a history of adverse reactions to celery root. *J Allergy Clin Immunol*, **106**(2): 373–378.

Central Statistics Office (CSO) (2015) *CensusAtSchool 2015*. Cork: Central Statistics Office. Available at: http://pdf.cso.ie/www/pdf/20160307101157_CensusAtSchool_2015_full.pdf

Cianferoni A and Muraro A (2012) Food-induced anaphylaxis. *Immunol Allergy Clin North Am*, **32**(1): 165–195.

Coeliac Society of Ireland (2018) Available at: https://www.coeliac.ie/

Collin P, Thorell L, Kaukinen K and Mäki M (2004) The safe threshold for gluten contamination in gluten-free products. Can trace amounts be accepted in the treatment of coeliac disease? *Aliment Pharmacol Ther*, **19**: 1277–1283.

Crevel RW, Baumert JL, Baka A, Houben GF, Knulst AC, Kruizinga AG, Luccioli S, Taylor SL and Madsen CB (2014) Development and evolution of risk assessment for food allergens. *Food and Chemical Toxicology*, **67**: 262–276.

European Commission (2002) Regulation (EC) No. 178/2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety. Brussels: European Commission.

European Food Safety Authority (EFSA) Panel on Dietetic Products, Nutrition and Allergies (NDA) (2014) Scientific Opinion on the evaluation of allergenic foods and food ingredients for labelling purposes. *EFSA Journal*, 12(11): 3894.

European Union (2011) Regulation (EU) No 1169/2011 on the provision of food information to consumers. Brussels: European Union.

European Union (2014) Commission Implementing Regulation (EU) No 828/2014 on the requirements for the provision of information to consumers on the absence or reduced presence of gluten in food.

Food Safety Authority of Ireland (FSAI) (2012) *Audit of Irish Food Manufacturer Allergen Controls and Labelling*. Dublin: Food Safety Authority of Ireland. Available at: https://www.fsai.ie/uploadedFiles/Enforcement_and_Audit/Audit/Reports/Control_and_Labelling_Allergens_Catering_Est.pdf

Government of Ireland (2014a) S.I. No. 556/2014 European Union (Provision of Food Information to Consumers) Regulations 2014. Available at: http://www.irishstatutebook.ie/eli/2014/si/556/made/en/print?q=556&years=2014

Government of Ireland (2014b) S.I. No. 489/2014 Health (Provision of Food Allergen Information to Consumers in respect of Non-Prepacked Food) Regulations 2014. Available at: *http://www.irishstatutebook.ie/eli/2014/si/489/made/en/print?q=489&years=2014*

Grabenhenrich LB, Dölle S, Moneret-Vautrin A, Köhli A, Lange L, Spindler T, Ruëff F, Nemat K, Maris I, Roumpedaki E, Scherer K, Ott H, Reese T, Mustakov T, Lang R, Fernandez-Rivas M, Kowalski ML, Bilò MB, Hourihane JO, Papadopoulos NG, Beyer K, Muraro A and Worm M (2016) Anaphylaxis in children and adolescents: The European Anaphylaxis Registry. *J Allergy Clin Immunol*, **137**(4): 1128–1137.e1. Available at: https://doi.org/10.1016/j.jaci.2015.11.015

HIPE 1 (Hospital Inpatient Enquiry), Information Management Unit (IMU), Hospital Inpatient Enquiry (HIPE) database, Republic of Ireland. Discharges with a principal diagnosis of ICD-9-CM 995.60 - 995.69.

HIPE 2 (Hospital Inpatient Enquiry), Information Management Unit (IMU), Hospital Inpatient Enquiry (HIPE) database, Republic of Ireland. Discharges with a principal diagnosis of ICD-10, T780.

Huang F, Chawla K, Järvinen KM and Nowak-Węgrzyn A (2012) Anaphylaxis in a New York City paediatric emergency department: Triggers, treatments, and outcomes. *J Allergy Clin Immunol*, **129**(1): 162–168.

Irish Food Allergy Network (IFAN) (2018) Food allergy in summary. Available at: http://ifan.ie/food-allergy-in-summary/summary/

Kelleher MM, Dunn-Galvin A, Gray C, Murray DM, Kiely M, Kenny L, McLean WHI, Irvine AD and Hourihane JO (2016) Skin barrier impairment at birth predicts food allergy at 2 years of age. *J Allergy Clin Immunol*, **137**(4): 1111–1116.

Kruizinga AG, Briggs D, Crevel RW, Knulst AC, van den Bosch LM and Houben GF (2008) Probabilistic risk assessment model for allergens in food: sensitivity analysis of the minimum eliciting dose and food consumption. *Food and Chemical Toxicology*, **46**: 1437–1443.

Lyons J and Giltinan M (2013) The Irish Portion Sizes Database. Available at: www.iuna.net

Lyons J, Walton J and Flynn A (2013) Development of an online database of typical food portion sizes in Irish population groups. *J Nutr Sci*, 2: e25. Available at: https://dx.doi.org/10.1017%2Fjns.2013.14

Madsen CB, Hattersley S, Buck J, Gendel SM, Houben GF, Hourihane JO, Mackie A, Mills EN, Nørhede P, Taylor SL and Crevel RW (2009) Approaches to risk assessment in food allergy: report from a workshop "developing a framework for assessing the risk from allergenic foods". *Food and Chemical Toxicology*, **47**: 480–489.

Taylor SB, Christensen G, Grinter K, Sherlock R and Warren L (2018) The Allergen Bureau VITAL Program. *Journal of AOAC International*, **101**: 77–82.

United States Department of Agriculture (USDA) (2018) USDA National Nutrient Database. Available at: https://ndb.nal.usda.gov/ndb/search/list?home=true

APPENDIX 1

Food information to consumers Regulation (EU) No 1169/2011 – ANNEX II

SUBSTANCES OR PRODUCTS CAUSING ALLERGIES OR INTOLERANCES

1. Cereals containing gluten, namely: wheat, rye, barley, oats, spelt, kamut or their hybridised strains, and products thereof, except:
   (a) wheat-based glucose syrups including dextrose;
   (b) wheat-based maltodextrins;
   (c) glucose syrups based on barley;
   (d) cereals used for making alcoholic distillates including ethyl alcohol of agricultural origin;
2. Crustaceans and products thereof;
3. Eggs and products thereof;
4. Fish and products thereof, except:
   (a) fish gelatine used as carrier for vitamin or carotenoid preparations;
   (b) fish gelatine or Isinglass used as fining agent in beer and wine;
5. Peanuts and products thereof;
6. Soybeans and products thereof, except:
   (a) fully refined soybean oil and fat;
   (b) natural mixed tocopherols (E306), natural D-alpha tocopherol, natural D-alpha tocopherol acetate, and natural D-alpha tocopherol succinate from soybean sources;
   (c) vegetable oils derived phytosterols and phytosterol esters from soybean sources;
   (d) plant stanol ester produced from vegetable oil sterols from soybean sources;
7. Milk and products thereof (including lactose), except:
   (a) whey used for making alcoholic distillates including ethyl alcohol of agricultural origin;
   (b) lactitol;
8. Nuts, namely: almonds (*Amygdalus communis* L.), hazelnuts (*Corylus avellana*), walnuts (*Juglans regia*), cashews (*Anacardium occidentale*), pecan nuts (*Carya illinoinensis* (Wangenh.) K. Koch), Brazil nuts (*Bertholletia excelsa*), pistachio nuts (*Pistacia vera*), macadamia or Queensland nuts (*Macadamia ternifolia*), and products thereof, except for nuts used for making alcoholic distillates including ethyl alcohol of agricultural origin;
9. Celery and products thereof;
10. Mustard and products thereof;
11. Sesame seeds and products thereof;
12. Sulphur dioxide and sulphites at concentrations of more than 10 mg/kg or 10 mg/litre in terms of the total SO_2 which are to be calculated for products as proposed ready for consumption or as reconstituted according to the instructions of the manufacturers;
13. Lupin and products thereof;
14. Molluscs and products thereof.

APPENDIX 2

Further details on the 14 regulated food allergens (EFSA, 2014)

1. Peanut

Peanut (*Arachis hypogea*) is a member of the legume family of plants that includes peas, beans, soybeans, lupins, lentils and Fenugreek. Peanut consumption has increased in recent decades, most likely because it consists of easily digested proteins and is a versatile food ingredient. It can be consumed raw as a vegetable, crushed or ground as "butter", roasted or salted as a snack, incorporated into candies, and used to produce oil, which is extracted by using solvents or pressure. The use of peanuts and derived products in processed foods increases the risk of inadvertent exposure. Peanut allergies are more likely to be persistent, unlike other food allergies that may resolve with age.

Allergenic proteins identified in peanut

Allergen	Biochemical name	Superfamily/family	Molecular weight[a]
Ara h 1	7S Globulin (vicilin-type)	Cupin	64
Ara h 2	Conglutin (2S albumin)	Prolamin	17
Ara h 3	11S Globulin (legumin)	Cupin	60.34 (fragment)
Ara h 5	Profilin	Profilin	15
Ara h 6	Conglutin (2S albumin)	Prolamin	15
Ara h 7	Conglutin (2S albumin)	Prolamin	15
Ara h 8	PR-10	Bet v 1	17
Ara h 9	ns-LTP	Prolamin	9.8
Ara h 10	Oleosin	Oleosin	16[b]
Ara h 11	Oleosin	Oleosin	14[b]
Ara h 12	Defensin	–	8 kDa (reducing) 12 kDa (non-reducing) 5.184 kDa (mass)
Ara h 13	Defensin	–	8 kDa (reducing) 11 kDa (non-reducing) 5.472 kDa (mass)

[a]: Molecular weight (SDS-PAGE)

[b]: kDa

People who are allergic to peanuts show extensive cross-reactivity to other plants in the legume family, including peas, beans, clover, lupins and lentils. The peanut allergen Ara h 2 may be responsible for the cross-reactivity between peanuts, Brazil nuts and almonds due to shared epitopes. High-temperature treatment of peanuts can either increase (dry roasting) or decrease (moist heating) their allergenicity.

2. Nuts

Eight types of tree nuts are listed in Annex II of the FIC Regulation: almonds, hazelnuts, walnuts, cashews, pecan nuts, Brazil nuts, pistachio nuts and macadamia (Queensland) nuts. Although some outgrow their allergy, most people diagnosed with a tree nut allergy must avoid those nuts for life. It has been estimated that nuts and peanuts represent the triggering factor for about one-third to one-quarter of all anaphylactic reactions attributed to food consumption (Cianferoni and Muraro, 2012; Huang *et al*., 2012). Allergy to one type of tree nut (and peanuts) is a risk factor for developing allergy to other types of nuts.

The majority of nut allergens are seed storage proteins, such as vicilins, legumins and 2S albumins. Other nut allergens include pathogenesis-related proteins (chitinases, Bet v 1 homologues and lipid transfer proteins) and structural proteins (profilins and oleosins). Profilins are pan-allergens (present in pollens, nuts, seeds, fresh fruit and other vegetables). Proteins that have more recently been identified as tree nut allergens include manganese superoxide dismutase, 60S acidic ribosomal protein P2, and cytosolic small heat shock protein. Allergy to hazelnut and almond – and, less frequently, to other nuts – can be induced by sensitisation to birch pollen, plane tree pollen or mugwort pollen. Subjecting tree nuts to thermal and other processing techniques can have an effect on the allergenicity of the nut.

3. Egg

Annex II of the FIC Regulation does not distinguish between eggs from different avian species and so it is understood to include eggs from all birds used in food production, including domestic chickens, ducks and geese, among others. However, much of the research into egg allergies has been carried out on eggs from the domestic chicken (*Gallus gallus domesticus*).

Allergenic proteins identified in egg

Fraction	Allergen	Biochemical name	Concentration (%)	Molecular weight[a]
Egg white	Gal d 1	Ovomucoid	11	28
	Gal d 2	Ovalbumin	54	44
	Gal d 3	Ovotransferrin	13	78
	Gal d 4	Lysozyme C	3.5	14
Egg yolk	Gal d 5	Serum albumin	48	69
	Gal d 6	(α-livetin)		
		YGP42	–	35[b]

[a]: Molecular weight (SDS-PAGE)

[b]: kDa

In Western countries, allergies to egg, peanuts and milk are the most frequent food allergies in childhood, although many children grow out of egg allergy. Ovomucoid, a highly glycosylated protein with trypsin inhibitory properties, is one of the more clinically significant egg allergens and is found in the egg white.

4. Milk

Bovine milk typically contains between 31 g and 36 g of protein per litre. The two major groups of protein found in milk are casein and whey. Whey is mostly produced as a by-product of cheese, strained yoghurt or casein production; however, in more recent years, membranes have also been used to separate whey from casein. Individual, and/or combinations of, casein and whey proteins have been associated with cow's milk allergy (EFSA, 2014) to varying extents.

Allergenic proteins identified in milk

Allergen	Biochemical name	Concentration (g/L)	Molecular weight[b]	pI[c]
Whey proteins		**~5.0**		
Bos d 4	α-Lactalbumin	1–1.5	14.2	4.8
Bos d 5	β-Lactoglobulin	3–4	18.3	5.3
Bos d 6	Bovine serum albumin	0.1–0.4	67.0	4.9–5.1
Bos d 7	Immunoglobulin	0.6–1.0	160.0	–
Bos d lactoferrin	Lactoferrin[1]	0.09	80.0	8.7
Caseins		**~30**		
Bos d 8		20–30		
Bos d 9	α_{s1}-Casein	12–15	23.6	4.9–5.0
Bos d 10	α_{s2}-Casein	3–4	25.2	5.2–5.4
Bos d 11	β-Casein	9–11	24.0	5.1–5.4
NA	γ_1-Casein[a]	1–2	20.6	5.5
NA	γ_2-Casein[a]		11.8	6.4
NA	γ_3-Casein[a]	3–4	11.6	5.8
Bos d 4	κ-Casein		19.0	5.4–5.6

[a] www.allergome.org

[b] Molecular weight (SDS-PAGE)

[c] Isoelectric point

NA = not assigned

Due to the large variability observed in human IgE response, no single protein or protein structure is considered to account for a major part of milk allergenicity. Heat treatments can decrease or increase the allergenicity of milk allergens, depending on the temperature and duration of the treatment. Fermentation and hydrolytic processes may decrease allergenicity depending on the microorganisms used and the reaction conditions.

5. Cereals containing gluten

Coeliac disease is an autoimmune systemic disorder triggered by gluten in genetically susceptible individuals and is estimated to affect almost 1% of the Irish population (Coeliac Society of Ireland, 2018). Coeliac disease has a wide range of clinical presentations in all age groups and the only way of managing it is by avoiding cereals containing gluten in the diet. Gluten is the rubbery dough-forming protein fraction that remains when wheat flour is washed to remove starch. Gluten consists primarily of the seed-storage proteins glutenin and gliadin, which have been shown to trigger the pathophysiological and clinical features of coeliac disease. Cereals containing gluten included in Annex II of the FIC Regulation are varieties of wheat, rye, barley, spelt, kamut and oats. Although the association of oats with coeliac disease has not been firmly established, the primary reason for its inclusion is the risk of cross-contamination with gluten from wheat and barley. The negative impact of gluten on people with coeliac disease is not altered by most food processing techniques.

6. Fish

Fish and fish products are a common cause of severe and even fatal reactions. Like eggs and milk, there is no distinction between the many possible fish types in Annex II of the FIC Regulation. Allergy to fish is generally observed in young children but can also manifest in later life. Parvalbumin is a significant fish allergen found in all fish species. Fish muscle and fish skin are found to share allergens; however, fish roe has allergens that are found neither in fish muscle nor fish skin.

Allergenic proteins identified in fish (*Animalia Chordata*)

Biochemical name	Allergen	Common name	Scientific name	Source	Molecular weight[a]
β-Parvalbumin	Clu h 1 Cyp c 1 Gad c 1 Gad m 1 Lat c 1 Lep w 1 Onc m 1 Sal s 1 Sar s 1 Seb m 1 Thu a 1 Xip g 1	Atlantic herring Carp Codfish Atlantic cod Barramundi Whiff Rainbow trout Atlantic salmon Pacific pilchard Ocean perch Yellowfin tuna Swordfish	*Clupea harengus* *Cyprinus carpio* *Gadus callarias* *Gadus morhua* *Lates calcarifer* *Lepidorhombus whiffiagonis* *Oncorhynchus mykiss* *Salmo salar* *Sardinops sagax* *Sebastes marinus* *Thunnus albacares* *Xiphias gladius*	Fish meat	12[b]
Tropomyosin	Ore m 4	Mozambique tilapia	*Oreochromis mossambicus*	Fish meat	33[c]
β-Enolase	Gad m 2 Sal s 2 Thu a 2	Atlantic cod Atlantic salmon Yellowfin tuna	*Gadus morhua* *Salmo salar* *Thunnus albacares*	Fish meat	47.3[c] 47.3[c] 50
Aldolase A	Gad m 3 Sal s 3 Thu a 3	Atlantic cod Atlantic salmon Yellowfin tuna	*Gadus morhua* *Salmo salar* *Thunnus albacares*	Fish meat	40 40 40
Vitellogenin (β' component)	Onc k 5	Chum salmon	*Oncorhynchus keta*	Fish roe	18[b]

[a]: Molecular weight (SDS-PAGE)

[b]: Approximate – slight variation exists between species

[c]: kDa

7. Sesame seed

Sesame is cultivated mainly for its seeds, which are used in a range of foods, and for its seed oil, of which 50–60% of the seed is composed. Allergies to sesame seeds seem to persist, like those to fish and peanuts. People with an allergy to sesame seeds are likely to have multiple food allergies, particularly to peanuts and tree nuts.

8. Crustaceans

Decapod crustaceans (e.g. shrimp, prawn, crab and lobster) are of primary concern as allergenic foods, although some non-decapod crustaceans, such as krill, mantis shrimp and barnacles, have more recently been identified as allergenic.

There are 30 different allergenic proteins in crustaceans, the major ones being tropomyosin, arginine kinase, sarcoplasmic calcium-binding protein, myosin light chain 1 and myosin light chain 2. There can be significant cross-reactivity between different crustaceans, as well as with some fish.

Allergenic proteins identified in Crustaceans (*Animalia Arthropoda*)

Biochemical name	Allergen	Common name	Scientific name	Molecular weight[a]
Tropomyosin	Cha f 1 Cra c 1 Hom a 1 Lit v 1 Mac r 1 Met e 1 Pan b 1 Pan s 1 Pen a 1 Pen i 1 Pen m 1 Por p 1	Crab Common shrimp American lobster European white shrimp Giant freshwater prawn Greasyback shrimp Northern red shrimp Spiny lobster Brown shrimp Indian shrimp Black tiger prawn Blue swimmer crab	*Charybdis feriatus* *Crangon crangon* *Homarus americanus* *Litopenaeus vannamei* *Macrobrachium Rosenbergii* *Metapenaeus ensis* *Pandalus borealis* *Panulirus stimpsoni* *Panulirus stimpsoni* *Penaeus indicus* *Penaeus monodon* *Portunus pelagicus*	34 38[b] – 36 37[b] – 37[b] 34 36 34 38 39[b]
Arginine kinase	Cra c 2 Lit v 2 Pen m 2	Common shrimp European white shrimp Black tiger prawn	*Crangon crangon* *Litopenaeus vannemei* *Penaeus monodon*	45[b] 40
Myosin light chain 2	Hom a 3 Lit v 3 Pen m 3	American lobster European white shrimp Black tiger prawn	*Homarus americanus* *Litopenaeus vannemei* *Penaeus monodon*	23 20
Sarcoplasmic calcium-binding protein (SCBP)	Cra c 4 Lit v 4 Pen m 4 Pon 1 4	Common shrimp European white shrimp Black tiger prawn Narrow clawed crayfish	*Crangon crangon* *Litopenaeus vannemei* *Penaeus monodon* *Pontastacus leptodactylus*	25 20 – 24[b]
Myosin light chain 1	Art fr 5 Cra c 5	Brine shrimp Common shrimp	*Artemia franciscana* *Crangon crangon*	17.5 17.5
Troponin C	Cra c 6 Hom a 6 Pen m 6	Common shrimp American lobster Black tiger prawn	*Crangon crangon* *Homarus americanus* *Penaeus monodon*	21 20 –
Troponin 1	Pon 1 7	Narrow clawed crayfish	*Pontastacus leptodactylus*	30[b]
Triosephosphate isomerase	Arc s 8 Cra c 8	Shrimp Common shrimp	*Archaeopotambius siberiensis* *Crangon crangon*	28[b] 28

[a]: Molecular weight (SDS-PAGE). Approximate – some variation exists between species.

[b]: kDa

9. Soybean

Soybean is an edible legume with seeds containing approximately 20% oil and 40% protein. Human and animal consumption of soybeans and derived products has increased in the EU in recent decades. Human exposure to soybeans is largely due to the ubiquitous availability of processed food in which soy protein constitutes a considerable amount of the overall protein source. Allergic reactions to soy are generally mild (EFSA, 2014). Serological cross-reactivities have been observed with other legumes such as peanuts, green peas, lima beans and string beans.

Allergenic proteins identified in soybean

Allergen	Protein	Molecular weight[a]	Superfamily/family
Gly m 1	Hydrophobic protein	7	Hydrophobic seed protein
Gly m 2	Defensin	8	Defensin
Gly m 3	Profilin	14	Profilin
Gly m 4	PR-10 protein	17	Bet v 1 related protein
Gly m 5	β-Conglycinin (7S globulin, vicilin) Subunit α Subunit α' Subunit β	67 71 50	Cupin
Gly m 6	Glycinin (11S globulin, legumin) Subunit Gy1 Subunit Gy2 Subunit Gy3 Subunit Gy4 Subunit Gy5	 53.6 52.4 52.2 61.2 55.4	Cupin
Gly m 7	Seed biotinylated protein	76.2[b]	
Gly m 8	2S Albumin	28	Prolamin

[a]: Molecular weight (SDS-PAGE)

[b]: kDa

10. Molluscs

Molluscs are commonly classified into eight classes, of which three are of particular importance as food, namely gastropods, bivalves and cephalopods. The largest class, *Gastropoda*, consists of more than 70,000 species. In molluscs, the major allergen is tropomyosin, and minor allergens include hemocyanin, myosin heavy chain, arginine kinase, and amylase. Anaphylactic reactions and death have been reported in mollusc-allergic patients, including cases of food-dependent exercise-induced anaphylaxis. Allergies to molluscs are found to generally develop later in life (among school-going children and young adults), which is possibly a feature of the timing of molluscs' introduction to the human diet as well as of cross-reactive respiratory allergies.

11. Celery

Celery tuber/root is an important source of food allergens in Central Europe and can be found in many processed foods throughout the EU due to its aromatic flavour. People with an allergy to birch pollen are at a greater risk of being allergic to celery. For the purposes of allergen labelling, celeriac is considered to be equivalent to celery.

12. Lupins

Lupin is a legume, which includes more than 450 species and is widely grown as a flowering plant for animal feed and farmland management. While the usual garden varieties are poisonous, some species (sweet lupins) are used as whole seed flour or lupin drinks. Lupin is considered a good source of protein and is frequently used in foods for people who are intolerant to gluten. Many of the people at risk of developing an allergy to lupin can also be allergic to peanuts, while there is also some evidence of cross-reactivity with other legumes such as soybeans, lentils, beans, chickpeas and peas.

13. Mustard

The mustard plant belongs to the *Brassicaceae* family. White/yellow mustard (*Sinapis alba L.*), black mustard (*Brassica nigra L.*) and brown/oriental mustard (*Brassica juncea L.*) are the main types of mustard seeds used in cuisine and food processing. Commercial mustard powder is usually a mix of ground white and black mustard seeds. White and brown seeds are blended to make English-style mustard. White mustard seeds are the main ingredient in North American mustard, whereas the brown seeds are mainly used in Europe and China. Black mustard is mostly used in Indian cuisine. Mustard oil is also widely used as edible oil and as a flavouring agent in India. Whole, ground, cracked, or crushed mustard seeds can be mixed with water, vinegar, lemon juice, wine, or other liquids, salt, and other flavourings and spices to create a paste or sauce ranging in colour from bright yellow to dark brown. Mustard consumption in different countries varies according to local food habits. The risk of severe reaction seems to be higher for adults than children, which is possibly related to the timing of the introduction of mustard to the diet.

14. Sulphites

Sulphites occur naturally in some foods as a consequence of fermentation (e.g. wine) or may be added as preservatives or colours (additives) to fruits, vegetables and alcoholic drinks (e.g. cider, wine and beer). In accordance with the FIC Regulation, sulphur dioxide (SO_2) and sulphites at concentrations of more than 10 mg/kg or 10 mg/L in terms of the total SO_2 must be declared as allergens when present in the final food. Adverse reactions to ingested sulphites are not immune mediated, with most characterised by respiratory problems (bronchospasm), occasionally severe, which can occur within minutes after ingestion of sulphite-containing foods. SO_2 and sulphites are to be calculated for products as proposed ready for consumption or as reconstituted according to the instructions of the manufacturers.

APPENDIX 3

Request for advice from the Scientific Committee

Ref number:

Topic title: Food allergen risk assessment

Date requested: 30 September 2016

Date accepted: 18 October 2016

Target deadline for advice: 2018

Form of advice required: A strategy for carrying out a risk assessment on the presence of undeclared allergens listed in Regulation (EU) No. 1169/2011

Background/context

Regulation (EU) No. 1169/2011 sets out a list of 14 allergens that must be declared in a particular way when used as ingredients to produce food in the EU. Two of these ingredients (gluten-containing cereals and sulphur dioxide/sulphites) are not classical allergens in that they do not elicit an IgE-mediated response in humans when ingested by susceptible consumers. They also differ from the other 12 allergens on the list in that their presence in food above a certain level triggers a requirement for declaration.

The consumption of food consisting of or containing the other 12 allergens on the EU list results in IgE-mediated reactions in susceptible consumers. These reactions can result in mild to severe health consequences, or even death, depending on the food ingredient involved and the individual themselves, among other circumstances.

The implementation and monitoring of the allergen declaration requirement varies within the different EU Member States' jurisdictions, leading to different risk assessment conclusions and therefore different risk management decisions, possibly putting susceptible consumers at risk.

In 2011, the FSAI posed a number of questions to EFSA asking for advice on the following questions:

1. The prevalence of each allergy in the European Union.
2. Recommendations for threshold concentrations of each allergen in food that would provide an acceptable level of protection for at-risk consumers.
3. An overview of risk assessment strategies for allergens by Member States, with recommendations for a harmonised approach.
4. The suitability, or otherwise, of qualitative and quantitative DNA-based tests (PCR) for the detection and quantification of food allergens in comparison with immunological (e.g. ELISA) or other methods.

Question 3 was deemed to be a risk management issue and therefore outside the remit of a risk assessment body such as EFSA. The final EFSA opinion was published in 2014.

Despite the extensive EFSA opinion of 2014, and the wealth of research and other data publicly available, the risk assessment and risk management of food allergens in the EU is not harmonised. In Ireland, there is no system in place where a Public Analyst Laboratory can automatically conclude on whether the presence of an undeclared food allergen is in compliance with, or in breach of, EU and Irish food law. The FSAI is frequently asked to carry out risk assessments on the undeclared presence of the 12 food allergens for which regulatory limits have not been set. Guidance on the following questions would greatly assist those risk assessments to reach a science-based conclusion and feed in to pragmatic risk management decisions.

Questions for the FSAI Scientific Committee:

1. What is the prevalence of all 14 food allergies in Ireland?
2. What are the minimum levels of each of the 12 food allergens that can trigger an adverse response in humans (eliciting doses)?
3. Analytical capacity for food allergen detection and quantification in the Public Analyst Laboratory is limited, which means that only some of the 14 allergens are sampled for analysis each year. In view of the information to be obtained in points 1 & 2, which of the 14 food allergens pose the greatest risk for Ireland?
4. In view of the information to be obtained in points 1, 2 & 3, what is the maximum level of undeclared allergen (of the 12 without specified thresholds) that would ensure a high level of protection for susceptible consumers?

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