



Workshop Report

Application of scientific criteria to food allergens of public health importance[☆]Y.J. Chung^a, S. Ronsmans^b, R.W.R. Crevel^c, G.F. Houben^d, R.J. Rona^e, R. Ward^{f,1}, A. Baka^{g,*}^a Nestlé Research Centre, Lausanne, Switzerland^b Coca-Cola Services, Brussels, Belgium^c Safety and Environmental Assurance Centre, Unilever, Colworth House, Sharnbrook, Bedford, UK^d The Netherlands Organisation for Applied Scientific Research TNO, Zeist, The Netherlands^e King's College London, Department of Psychological Medicine London, UK^f PepsiCo International, UK^g International Life Sciences Institute – ILSI Europe, Brussels, Belgium

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ABSTRACT

Scientific criteria for identifying allergenic foods of public health importance (Björkstén, B., Crevel, R., Hischenhuber, C., Løvik, M., Samuels, F., Strobel, S., Taylor, S.L., Wal, J.-M., Ward, R., 2008. Criteria for identifying allergenic foods of public health importance. *Regulatory Toxicology and Pharmacology* 51(1), 42–52) have been further refined to incorporate an assessment of the strength of available scientific evidence (van Bilsen, J.H., Ronsmans, S., Crevel, R.W., Rona, R.J., Przyrembel, H., Penninks, A.H., Contor, L., Houben, G.F., 2011. Evaluation of scientific criteria for identifying allergenic food of public health importance. *Regulatory Toxicology and Pharmacology* 60, 281–289). A multi-disciplinary group was invited to critically test the refined approach. They independently evaluated selected publications on coconut, soy and/or peanut allergy, scored them using the newly developed level of evidence criteria, and debated proposed approaches for combining and utilising the scores to measure the overall impact of an allergen in public health impact assessments. The evaluation of selected publications using the modified criteria produced a relatively consistent result across the experts. These refined criteria were judged to be a way forward for the identification of allergenic foods of public health importance, and for prioritisation of allergen risk management and future data gathering. The debate to combine available evidence when assessing whether an allergenic food is of sufficient public health importance to warrant active management led to proposals on how to weight and combine evidence on allergen severity, potency and prevalence. The refined criteria facilitate a debate to find a meaningful sequence of steps to summarise the available information in relation to a food allergen.

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Abbreviations: DBPCFC, double blind placebo-controlled food challenge; ED 50, eliciting dose 50; FAO, Food and Agriculture Organisation; FARRP, Food Allergy Research and Resource Programme; IgE, immunoglobulin E; ILSI, International Life Sciences Institute; IUIS, International Union of Immunological Societies; JEFCA, The Joint FAO/WHO Committee on Food Additives; LOAEL, lowest-observed-adverse-effect-level; SBPCFC, single-blind, placebo-controlled food challenge; SPT, skin prick test; WHO, World Health Organisation.

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1. Introduction

Food allergy has been recognised by food safety authorities as a public health concern. In 1995 at the time the list of the most common allergenic foods was drawn up by the World Health Organization (WHO) (FAO 1995; Codex, 1999), information on prevalence and severity was used, but available data was very limited. Since then, well-documented cases of allergic reactions to numerous allergenic foods have been reported, (FAO, 1995; Hefle, Nordlee, and Taylor, 1996; Taylor, 2000; EFSA, 2004; Burks et al., in press). Food allergen labelling lists currently vary widely across the globe (Gendel, 2012), usually based on the Codex list (Codex, 1999). Addition of allergenic foods to local labelling lists does not follow a harmonised approach in risk assessment and risk management decision-making, leading to confusion, and practical challenges for industry, consumers and public health agencies alike. Allergic consumers require appropriate and accurate risk communication of the allergenic potential of a given food to make sound judgments about avoiding foods to which they are sensitised (Sakellariou

et al., 2009; Barnett et al., 2011). Use of explicit scientific criteria to justify addition of foods to allergen lists would ensure public health protection measures are pertinent to local needs and protect allergic consumers.

In order to decide objectively if a food needs to be addressed as an allergenic food of public health importance, three questions have to be answered: Is the food allergenic? Is its allergenicity of public health significance? What is the quality of the data available to answer the previous two questions? With these questions in mind, an expert group appointed by the ILSI Europe Food Allergy Task Force proposed a set of scientific criteria together with a framework for their use (Björkstén et al., 2008). These criteria included clinical characterization (IgE-mediated reaction), potency of the allergen, severity of the reaction and prevalence in a population. In the framework, the quality of the evidence supporting each of these criteria in the available dataset (body of scientific literature) is assessed using a score that had been developed by discussion and consensus by an expert committee. Such criteria can be useful in making a decision as to whether sufficient quality data exist to evaluate individual allergenic foods regarding their level of public health significance. If so, the criteria can serve as a common basis for assessing and comparing the public health impact of allergens. If the criteria indicate that quality data are lacking, they have the benefit of pointing out the direction in which more research is needed to be able to perform proper risk assessments. Efforts have been made elsewhere to develop objective criteria for the establishment of allergenic foods as a priority for public health, notably by Health Canada (Health Canada, 2010). An example of applying these criteria was the recent evaluation by Health Canada of mustard and garlic, resulting in only mustard having been added to the Canadian priority food allergen list (Health Canada, 2009a,b; Health Canada, 2010).

Further refinement of the original scientific criteria developed by Björkstén et al., 2008) has been performed recently (van Bilsen et al., 2011). A partnership between ILSI Europe and TNO aimed to test and review the application of the proposed criteria (Björkstén et al., 2008) to assess whether this approach could be widely used, and to further evaluate whether the criterion and the descriptors for the quality of evidence were unambiguous and covered the full range of type and levels of evidence in the literature. The resulting refinement of the descriptors provided guidance on how to interpret the literature in terms of strength of the evidence and demonstrated that the criteria framework could discriminate between high, moderate and low quality of evidence. It also reaffirmed the benefits of having objective scientific criteria in a structured framework to support a harmonised and consistent scientific approach, and thus provides an explicit basis for future assessments of allergenic foods to risk assessors and risk managers with a varied range of experience of food allergy. While this framework establishes a common basis regarding the scientific evidence to be included in an allergens risk assessment exercise, it does not provide an actual evaluation of the public health relevance of that allergen.

In practice, public health assessments always have to use the data available at the time. As such, using this framework allows for assessing the available information taking into account its quality, and provides the basis for carrying out a systematic review of the evidence regarding a specific allergen. Performing such assessments on a set of known and potentially new allergens, will allow identification of data gaps in science, if any. Subsequently such assessments allow for an exercise in prioritisation according to relevance for public health, comparing food allergens relative to each other. The relevant parameters for doing so are prevalence in the local population, potency of the allergen and severity of adverse reactions.

The ILSI Europe Food Allergy Task Force organised a workshop in September 2010 primarily to further assess the applicability, completeness and ease of use of the approach. A range of potential users of the scientific criteria framework (i.e. government risk assessors and risk managers, regulators, public health scientists, industry risk managers) not involved in the development of the criteria were invited to the workshop. The experts were asked to undertake an independent evaluation of selected scientific publications on several foods using the scientific criteria developed and refined (Björkstén et al., 2008; van Bilsen et al., 2011). In other words, the usability and value of these criteria were assessed on data on several foods.

Having invited a great variety of experts to the workshop for validating the applicability of the proposed criteria for the evaluation of the strength of scientific evidence, the workshop also performed an initial brainstorming exercise, on how one could approach an assessment of public health impact of existing and emerging allergens. Based on the feedback received, this report contains suggestions that will be useful to initiate further work in that area. This paper presents the process, outcome and recommendations emerging during the workshop.

2. Workshop methodology approach

2.1. Application of the modified criteria to a selected set of scientific publications

The first element of the workshop review was to examine how consistently the modified criteria and quality of descriptors (van Bilsen et al., 2011) could be applied to a selection of food items as reported in the scientific literature. Scientific papers on three known or emerging allergenic foods (peanut, coconut and soybean) were chosen by the Expert Group for this exercise. Peanut was chosen as the initial case study for evaluation as a well-known and broadly investigated allergen, with documented severe reactions at low doses. Two further and contrasting examples were chosen for the workshop evaluation – soy as an allergen with much higher thresholds for elicitation of adverse reactions, and coconut as a potential emerging allergen. The scientific papers were sourced from the scientific literature database developed in the previous work done by the expert group and TNO, utilising the Food Allergy Research and Resource Program (FARRP, University of Nebraska) database on allergenic foods, and the US National Library of Medicine's Medline service, using prescribed search keywords as described in van Bilsen et al. (2011). The publications provided for review for each allergen are listed in the Appendix.

Scientific experts were invited from different stakeholder groups, (i.e. food industry, governments, academia, research organization, and consumer protection), and from a wide range of scientific fields, (e.g. clinicians, biochemists, toxicologists, food scientists, epidemiologists, public health scientists). A list of the participants can be found on www.ils.eu. Each invited scientist was asked to assess and score the quality (strength) of evidence for a set of scientific papers for each of two out of three chosen allergenic foods (peanut, soy and/or coconut) using the defined criteria, and scoring them against the modified descriptors for levels of evidence (see Table 1). Each individual's findings were first combined and discussed in a single small group of 8–9 participants. After completing the scoring for quality of evidence for each criterion, the groups then shared their evaluations with a second group evaluating the same papers for the same allergenic food to compare consistency in scoring, highlight any ambiguity in interpretation and identify potential improvements/refinements. Each workgroup was represented by the experts in various fields. This review mechanic was felt to provide a practical test of the robustness, ease of use and clarity of the criteria and their descriptors for assessing level of evidence.

Table 1

Type and level (weight) of evidence of clinical data according to modified criteria – text in bold are the modifications described in van Bilsen et al. (2011) made to the original criteria described in Björkstén et al. (2008).

Data supporting	Type of evidence	Level of evidence
IgE-mediated mechanism	At least two studies from independent centres, each based on at least one patient, in which the patient samples and food proteins are well defined ^a , demonstrating the presence of bound IgE antibodies and/or a positive SPT ^b	1
	At least two studies from independent centres, each based on at least one patient, in which the patient samples and food proteins are not well defined, demonstrating the presence of bound IgE antibodies and/or a positive SPT^b	2
	At least two serological studies showing specific IgE binding to foods/extracts and/or a positive SPT	3
	At least two studies of small numbers of serum samples from patients who are not adequately characterised	4
Adverse reactions caused by IgE-mediated mechanisms	DBPCFC ^{c,d} studies in well-characterised patients with defined doses of specific food ^a in well-described matrix ^e and with specific bound IgE antibodies and/or a positive SPT	1
	Series of patients with well-documented ^a history of reactions to suspected food, confirmed or not by DBPCFC ^c , and with specific bound IgE antibodies and/or a positive SPT	2
	Case reports of clinical symptoms and the presence of food-specific bound IgE antibodies and/or a positive SPT, but not confirmed by DBPCFC	3
	Elimination diets leading to resolution of symptoms	4
Potency	One or more threshold studies with good range of doses ^f and adequate numbers of unselected participants with documented clinical symptoms of allergy. Two or more level 2 threshold studies could add up to level 1	1
	Other threshold studies	2
	Case reports describing reactions to quantitatively estimated low doses	2
	Case reports describing reactions to qualitatively estimated low doses	3
Severity	Objective signs confirmed by physician, preferably classified according to scientifically accepted classification system	1
	Subjective symptoms reported by patient in DBPCFC study for repeated doses	2
	Subjective signs reported by patient in DPBCFC study at single dose	3
	Historical symptoms indicated by patient	4
Prevalence	Epidemiological studies in general community population, including verification of sensitization by IgE antibodies or positive SPT, presence of clinical symptoms and DBPCFC ^d	1
	As above but without DBPCFC ^d	2
	Epidemiological studies based on questionnaires for clinical symptoms and sensitization in the general population	2
	Epidemiological studies based on questionnaires for clinical symptoms or sensitization in the general population	3
	Surveys based on general clinics patients (e.g. general practitioners, children clinics)	4
	Registers of severe allergic reactions	4

^a Level of details sufficient to be reproducible.

^b Skin prick test, preferably performed according to the accepted Guidelines.

^c Double-blind placebo-controlled food challenge.

^d Or open challenges for infants.

^e Matrix with appropriate placebo control (with identical matrix composition as the matrix of active allergic material).

^f Dose-spacing should consist of doubling doses or involve a semi-logarithmic progression, starting at a dose low enough not to provoke a reaction in any participant. Moreover, no effect and effect level of clinical signs should be included.

2.2. Application of the findings in a public health impact assessment exercise

The second element of the workshop was to brainstorm and offer initial ideas on how the different scientific criteria, with varying strength of supporting evidence, could be incorporated into an overall assessment of the public health relevance of existing and emerging allergens. In order to facilitate the discussions, three different approaches were shared for critique at the workshop. The groups were asked to discuss the pros and cons for one option each, and, if possible, recommend additional options explaining the reasoning for a particular approach to a plenary feedback session.

3. Results

3.1. Application of the modified criteria to a selected set of scientific publications for coconut, soy and peanut

The workshop participants examined how consistently the modified criteria and quality of evidence descriptors developed

by ILSI Europe (Table 1; Björkstén et al., 2008; van Bilsen et al., 2011) could be applied to a selected dataset from the scientific literature. The results from individual assessments and group scores for each allergenic food considered are combined in Table 2 to describe the overall quality of evidence for each criterion provided by the scientific papers reviewed by the groups for all three allergenic foods. The evaluation of selected publications using the modified criteria produced a satisfactory degree of consistency across the experts. However, a few specific differences did arise in interpretation of the descriptors when scoring quality and weight of evidence for IgE-mediated hypersensitivity reactions.

Following review of a set of eight papers on coconut, it was concluded that evidence for IgE-mediated allergic reactions existed for coconut allergy, but data on prevalence and potency were lacking. Based on this dataset, more research appeared necessary, especially regarding data on prevalence. In discussion, the participants noticed that the discrepancy in the conclusions on the criterion of IgE-mediated mechanism as indicated in Table 2 (footnotes (a) and (b)) and Table 3 resulted from different interpretations of the relevant papers about the number of serum samples from patients. After discussion on the number of samples required to fulfil the cri-

Table 2

Summary of the overall level of agreement between groups on the level of quality of evidence of scientific publications.

Criteria	Level of quality of evidence					
	Coconut		Soybean		Peanut	
	Group 1	Group 2	Group 2	Group 3	Group 1	Group 3
IgE-mediated mechanism	1 ^a	3 ^b	2	1	2	1
Adverse reaction with IgE-mediated reaction	3	3	1	1	1	1
Potency	3	3	1	1	2	1
Severity	1	1	1	1	1	1
Prevalence	4 ^c	Not ranked ^d	Not ranked ^d	Not ranked ^d	2	2

^a At least two studies, in which the patient samples and food proteins are well defined, demonstrating the presence of bound IgE antibodies and/or a positive SPT.^b At least two studies of small numbers of serum samples from patients who are not adequately characterised.^c Registers of severe allergic reactions.^d Due to inapplicability of criteria to the data described in papers.**Table 3**

Details of the evaluations of scientific papers on coconut allergy.

Criteria	Rank	Papers evaluated																Overall rank	
		1		2		3		4		5		6		7		8			
		G1	G2	G1	G2	G1	G2	G1	G2	G1	G2	G1	G2	G1	G2	G1	G2	G1	G2
IgE	1	x										x						x	
	2																x		
	3		x			x	x	x	x				x			x			x
Adverse reaction	1																		
	2																		
	3	x	x			x	x	x	x			x	x			x		x	x
	4																		
Potency	1																		
	2																		
	3						x		x			x						x	x
Severity	1	x	x			x	x											x	x
	2																		
	3																		
	4																		
Prevalence	1																		
	2																		
	3																		
	4	x														x		x	

G1, group 1; G2, group 2; x denotes the level of quality of evidence agreed by the group assessing the evidence provided, where 1 is highest quality of evidence and 4 is the least (see Table 1).

Where a column is blank, the group found the information provided was insufficient to classify the quality of evidence.

terion for an IgE-mediated mechanism, it was concluded that the description “a small number of serum samples” for a level 3 quality of evidence was vague and that the number should be refined to state “serological studies with at least five samples” as the criteria to list a protein as an allergen (Chapman et al., 2007). The discrepancy in the conclusion on the criterion of prevalence, as indicated in Table 2 (footnotes (c) and (d)), resulted from the fact that group 1 considered a case report to be a registered severe allergic reaction whereas group 2 interpreted a case study as being a single case, which was not classifiable by the modified criteria. In any event, both groups identified that there was inadequate data to assess prevalence. Scoring of the quality of evidence provided by single case studies was also discussed. Although participants agreed that serological analyses made in single case studies could be of excellent quality, they could not be scored as level 1 for the purposes of establishing an IgE-mediated mechanism, as they had, by definition, not been reproduced. Such high-quality studies, however, are important in identifying emerging or new allergens. The allergenicity of a large number of foods is supported only by serological evidence such as cross-reactivity, identification of IgE binding proteins, and/or skin prick tests, without oral challenge studies. Although single oral challenge case studies can, by their nature, provide only limited data on prevalence, they can serve

as useful signals and are therefore meaningful in identifying emerging allergens.

The evaluation of the pre-selected articles on soy allergy is described in Table 4. The conclusions of both groups were similar overall, with a difference in scoring on the IgE-mediated mechanism resulting from the different interpretation of each group regarding the number of qualifying studies. One group ranked the criterion on IgE-mediated mechanism as a level 2, based on their finding that only one of the supplied studies qualified as a level 1. The other group ranked the IgE criterion as a level 1, having concluded that more than one study qualified for a level 1 score. As a consequence, a discussion on the quality and quantity of the evaluated studies took place. One group took the approach that in a literature set in which only one study qualifies for a level 1 (and several other studies classify as sub-level 1), a resulting level 2 should be the conclusion. On the other hand, the other group classified two out of five studies as level 1 and therefore concluded that the same data warranted a final level 1 score. The different interpretations led the participants to recognise a need for harmonisation in determining final scores for the IgE criteria when combining the conclusions on several studies, if each individual study gave a different conclusion in terms of strength of evidence. It should be noted that this remark is also a result of the design

Table 4

Details of the evaluations of scientific papers on soybean allergy.

Criteria	Rank	Papers evaluated											
		1		2		3		4		5		Overall rank	
		G2	G3	G2	G3	G2	G3	G2	G3	G2	G3	G2	G3
IgE	1		X							X	X		X
	2	X										X	
	3			X		X							
Adverse reaction	1	X								X	X	X	X
	2		X										
	3					X							
	4												
Potency	1									X	X	X	X
	2		X				X						
	3												
Severity	1	X	X			X	X		X	X	X	X	X
	2												
	3												
	4												
Prevalence	1												
	2												
	3												
	4											nr*	nr*

G2, group 2; G3, group 3; x denotes the level of quality of evidence agreed by the group assessing the evidence provided, where 1 is highest quality of evidence and 4 is the least (see Table 1).

Where a column is blank, the group found the information provided was insufficient to classify the quality of evidence.

* nr, not ranked.

Table 5

Details of the evaluations of scientific papers on peanut allergy.

Criteria	Rank	Papers evaluated									
		1		2		3		4		Overall rank	
		G1	G3	G1	G3	G1	G3	G1	G3	G1	G3
IgE	1			X	X		X				X
	2	X				X				X	
	3		X								
Adverse reaction	1			X	X					X	X
	2						X				
	3										
	4										
Potency	1				X						X
	2			X						X	
	3										
Severity	1			X	X					X	X
	2										
	3						X		X		
	4							X			
Prevalence	1										
	2					X			X	X	X
	3										
	4										

G1, group 1; G3, group 3; x denotes the level of quality of evidence agreed by the group assessing the evidence provided, where 1 is highest quality of evidence and 4 is the least (see Table 1).

Where a column is blank, the group found the information provided was insufficient to classify the quality of evidence.

and context of the exercise, whereby only a few papers were provided to individual assessors.

The details and overall scoring of criteria for four selected articles on peanut allergy are shown in Table 5. Some discrepancies in the conclusions surfaced between assessors. Evaluation of the criteria for IgE-mediated mechanisms showed that one of the articles had data on a skin prick test using peanut protein extract. However, the source of the protein extract was not described in the article. In order for skin prick test (SPT) data to be credible, the source of protein extracts should be indicated in the papers and proteins from commercial sources would be sufficient for reproducibility

of the procedure. It was suggested that for the criteria on evidence for severity, subjective symptoms should be left out of the criteria of level 3 of evidence, as they are already considered level 2 of evidence. In addition, the importance of number of doses in the DBPCFC study was questioned, suggesting omission of the number (single or repeated) of doses from the descriptors of level 2 and 3 evidence. Only one out of the four studies on peanut allergy was suitable for assessing evidence of potency (i.e. how much is needed to trigger a reaction). For this study, the two groups ranked the evidence differently. The discrepancy arose from the interpretation of the number of studies. Whereas one group interpreted the study by

Hourihane et al. (2005) to involve two centres in two different studies, the other group considered the study by Hourihane et al. (2005) to be a single study in one centre. As a consequence, the first group attributed a top level 1 score to the study, whereas the second group ranked it at a level 2 with respect to the quality of evidence for this criterion. During the discussion, participants concluded that clarification was needed as to how to deal with the number of centres when scoring the quality of evidence for the criterion of potency. For example, the study by Hourihane et al. (2005) included several clinics that recruited allergic patients and one centre for food challenge studies. A minor modification of the descriptor for level 1 evidence for the potency criterion might be necessary to clarify the actual meaning of “at least two centres” in one study or one publication.

Besides the individual remarks made on the fine-tuning of the modified Björkstén et al. (2008) criteria by the groups, it was also proposed that in order to ensure applicability of the overall set of criteria, the criteria should be kept as simple and concise as possible. Usability of the criteria for risk assessors and managers in the food industry and government authorities needs to be kept in mind. It was concluded that a balance should be achieved between including too much detail in order to cover all possible scenarios and a lack of detail in the descriptors of the scoring which would not be able to capture the appropriate level of quality of evidence.

3.2. Approaches for utilising the criteria and strength of evidence for each element in an overall public health impact assessment

Following the evaluation of example papers on individual allergenic foods to identify the quality and weight of evidence of IgE-mediated allergy, the groups went on to explore how risk managers could ascertain whether the evidence available could be used to (i) indicate the overall public health importance of a food allergen in

contrast to its importance to the health of individuals with the allergy (e.g. risk of adverse reactions to a specific food), and (ii) discriminate between the impact of different allergenic foods on public health.

Three initial options were provided to prompt the brain-storming session:

Option 1: A weighted value approach. This approach aimed to capture and quantify for a given allergen, for each individual criterion, the combination of the strength of evidence that exists for this criterion and the actual level of findings (e.g. low versus high prevalence) that can be concluded upon for that criterion. To use this approach, one would need to develop a grading system to classify the level of findings for the different criteria. The strength of the scientific literature would follow from the modified Björkstén et al. classification. The overall final combined numerical score would be a possible way of prioritising allergens versus each other.

Option 2: A group analysis approach. This approach sought to map out two-dimensional charts, with the aim of comparing the prevalence in relation to the potency and severity of a given allergen respectively. Each allergen could then be positioned in one of the chart areas as a function of the two criteria being evaluated. By grading the domains of the chart in such a way, one can visualise the difference between several allergens, or one can use the numerical values attributed to the different chart areas. Both option 1 and option 2 approaches could be measures of the relative public health relevance of allergens.

Option 3: A high versus low priority approach. This approach simply ranks both the quality of evidence as well as the potential health relevance, as a qualitative descriptor: high or low. This simple approach could be valuable in a top-line prioritisation exercise, where one seeks to identify the priority allergens to

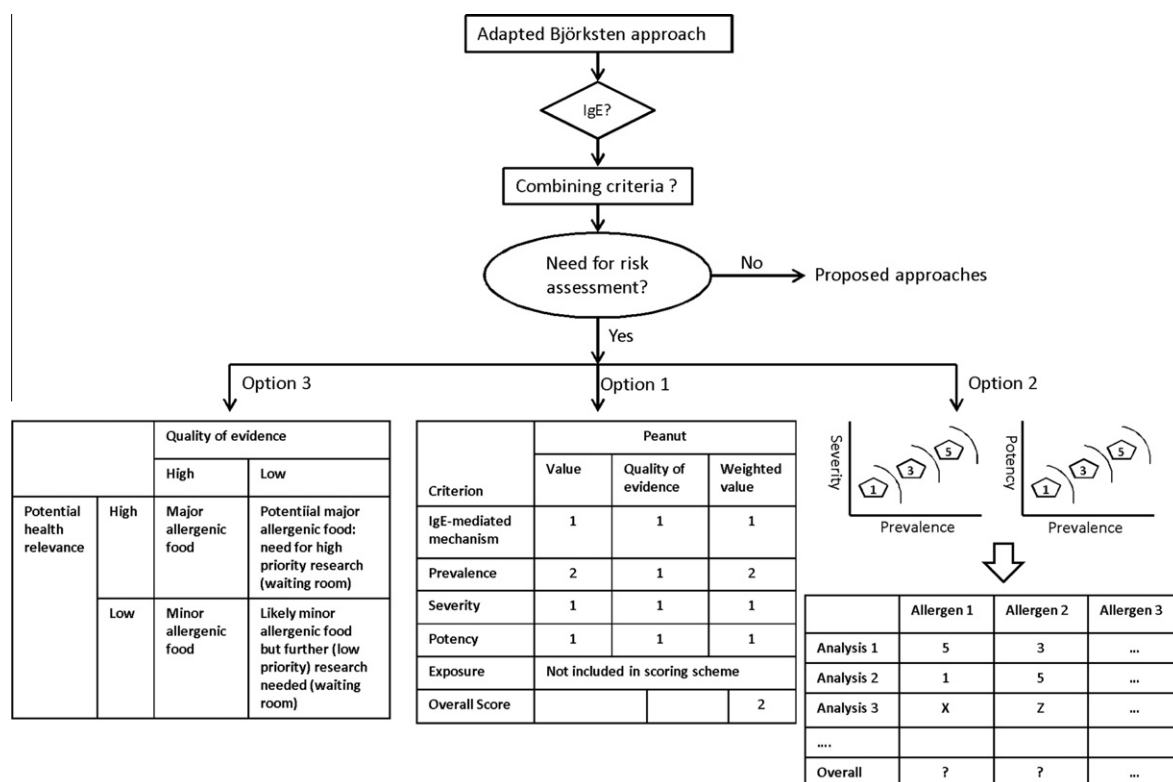


Fig. 1. Diagram illustrating options considered for public health impact assessment of allergenic foods.

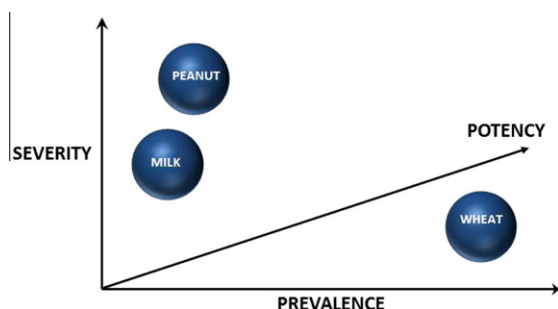


Fig. 2. Diagram illustrating the potential for three-dimensional relative positioning of allergenic foods against the three key criteria of potency, severity and prevalence.

work on, versus the ones that can be considered to be in the “waiting room” in terms of insufficient evidence, further research or regulatory measures. A schematic representation of the thinking behind each option is depicted in Fig. 1.

Combining the weighted value approach (option 1) and group analysis approach (option 2) was suggested as one way to express this evidence of likelihood of severe adverse reactions in such a way that it can discriminate between different foods of proven allergenicity (Fig. 2). Numerical scoring to rank individual allergenic foods was not viewed as feasible, given the disparate types of data, limited evidence usually available, and the uncertainty as to whether future studies would be able to cater for the missing gaps (either due to lack of funding or lack of sufficient allergic subjects available for challenge tests). Risk managers, however, still need to make decisions on public health importance using whatever data they have available. The group therefore tried to develop an alternative approach that would permit best use of any/all data available on known and future/emerging allergenic foods. Ideally, the approach would also permit observation of the impact of any changes over time.

The weighted value approach (option 1) combines quality of evidence and the “magnitude” of the findings themselves. It allows transparency of data used for decision making, however, the current scores describe levels of evidence and not level of public health concern. Thus, any number generated should be seen as an aid to decision making and not a definitive or comparative “score” for the impact of an allergenic food on public health. The group analysis approach (option 2) provided helpful visual representation of the impact of the criteria and could show how allergens were positioned relative to each other, but would not illustrate strength of evidence. The high versus low priority approach (option 3), may need more choices in scale to better translate the ILSI scientific criteria approach. In general, each option has its own merits and can complement the others. However, some participants were sceptical of the merits of any of these approaches.

To create a benchmark, data presentation using three-dimensional plots against prevalence, potency and severity was suggested for the existing regulated allergenic foods. A peanut allergy index of risk potential was suggested that could be used as the reference food item and other allergenic foods could be compared relative to this referent. Clustering could further provide additional information of impact due to any/all of the three vectors. Different populations and even potential at-risk subpopulations (e.g. those on restricted diets, such as vegetarians and diabetics) could be compared with the general population. Data gaps could then help identify areas for improvement in clinical and epidemiological data collection for food allergy public health decision making. The impact on quality of life in allergic patients’ also needs to be considered in the assessment and included into

the criteria. Combining criteria to derive a single estimate of public health impact has the potential to disregard important information. Thus decision making should not rely only on one summary estimate.

Further thinking in this area is needed and a new ILSI Europe expert group will continue to progress approaches for public health impact assessments for food allergens.

4. Discussion and conclusions

The workshop participants concluded that the modified criteria with the associated quality descriptors and scores for levels of evidence developed by ILSI Europe (Björkstén et al., 2008; van Bilsen et al., 2011), provide a practical approach for assessing the strength of evidence supporting the classification of food allergens. The assessment of scientific papers exercise was also felt to be practical and gave structure to a valuable discussion on assessing quality of evidence. The descriptors were judged to be helpful in determining the weight that should be accorded to each element of the available evidence.

The evaluation of selected publications for their weight of evidence according to the modified criteria based on the paper by Björkstén et al. (2008) was relatively consistent between groups of experts. Minor modifications in descriptors of the quality of evidence for each of the criteria would improve coherent application by users, such as clarifying the required number of serum samples for patients and guidance on interpretation of number of studies and number of centres. In addition, incorporation of inclusion criteria for eligible publications, as used by Health Canada for inclusion of new allergenic foods to their food allergen list was acknowledged as an existing precedent (Health Canada, The Canadian Criteria for the Establishment of New Priority Food Allergens, 2010).

The exercise demonstrated that agreement between experts is possible, but minor differences between assessors will remain due to type of expertise and variation in the ability to appraise the literature of food allergy. The structure of the ILSI Europe scientific criteria allows the use of all available data, but information for many (especially emerging) allergens is scarce and often of limited quality. The structure also allows identification of critical gaps in data for identifying allergenic foods of public health importance. Resources can then be allocated in the most effective way to address these data gaps.

The workshop confirmed that the three key criteria to establish the public health importance of an allergenic food would be potency, severity and prevalence.

- Potency could be preferably expressed as the ED50 (amount required to produce a reaction in 50% of a specific allergic population) or ED10 of the Minimum Eliciting Dose distribution or, if not available, the LOAEL (lowest observed adverse effect level). Differentiation according to type of effect is possible. Categorisation (allergens allocated in, e.g. low, medium or high potency categories) is also possible, but decisions on cut-offs are needed for that. Categorisation, if preferred, will be done later in the hazard assessment process because the expression of potency as a value gives more information.
- Severity of effects should be indicated in combination with their frequency in the population. Categorisation is possible as minor, moderate or severe, however further development of definitions would be needed. It was suggested that severity be expressed as incidence (%) of effects in a population.
- Prevalence of allergy can vary geographically and these differences should be listed as part of the hazard characterisation. It is a risk management decision whether or not to use the high-

est prevalence in any region. Patient recruitment and selection issues are possible. Prevalence is preferably expressed as the absolute prevalence in a population or as the relative (%) prevalence among food allergy patients.

It was recommended that potency, severity and prevalence as criteria should *not* be dealt with via a decision tree approach where conclusion on one criterion would determine whether another criterion is to be considered, but that all three criteria should be considered in a weight-of-evidence approach. A high prevalence of mild effects might, for instance, be as important as a very low prevalence of moderate/severe effects. Instead, a three-dimensional positioning of allergens could be used to illustrate the impact of different allergens relative to each other. Fig. 2 visually represents how this might be done. A critical consideration in combining data from different sources to determine the public health importance of an allergenic food is what weight (by importance) to attribute to each component. In this context, it is difficult to do this unless the risk management objectives are clearly set out first. In a societal context for example, does a very large number of fairly mild reactions count for the same as a few severe, life-threatening ones?

These refined criteria were judged to represent an improvement and be a way forward as an expert tool for the identification of food allergens of public health importance, and for prioritisation of allergen risk management and future data gathering. A full application of the modified (or simplified) quality of evidence descriptors to the literature on a known allergen would ensure the value of such criteria in risk assessment. Future work should now be done to apply and incorporate this scientific criteria framework into an overall weighted approach of establishing the actual public health importance of a given allergen.

Conflict of interest statement

The authors declare that there are no conflicts of interest.

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The opinions expressed herein and the conclusions of this publication are those of the authors based on the discussions with those attending the workshop and do not necessarily represent the views of ILSI Europe nor those of its member companies.

Appendix A. List of literature provided for each allergen

Coconut. allergy

Nguyen et al. (2004). Cross-reactivity between coconut and hazelnut proteins in a patient with coconut anaphylaxis. *Annals of Allergy, Asthma and Immunology* 92(2), 281–284.

Fiocchi et al. (2006). Food allergy and the introduction of solid foods to infants: a consensus document. *Annals of Allergy, Asthma and Immunology* 97(1), 10–21.

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Tella et al. (2003). A case of coconut allergy. *Allergy: European Journal of Allergy and Clinical Immunology* 58(8), 825–826.

Burks et al. (2001). Food allergens. *Current Opinion in Allergy and Clinical Immunology*, 1(3), 243–248.

Teuber and Peterson (1999). Systemic allergic reaction to coconut (*Cocos nucifera*) in 2 subjects with hypersensitivity to tree nut and demonstration of cross-reactivity to legumin-like seed storage proteins: New coconut and walnut food allergens. *Journal of Allergy and Clinical Immunology* 103(6), 118

Sicherer et al. (2003). Prevalence of peanut and tree nut allergy in the United States determined by means of a random digit dial telephone survey: a 5-year follow-up study. *Journal of Allergy and Clinical Immunology* 112(6), 1203–1207.

Rangsihienchai et al. (2009). Prevalence of coconut allergy in children with tree nut and peanut allergies. *Journal of Allergy and Clinical Immunology* 123, S26 (Abstract).

Soy. allergy

Bruno et al. (1997). Soy allergy is not common in atopic children: a multicenter study. *Paediatric Allergy and Immunology* 8(4), 190–193.

Codina et al. (2003). Allergenicity of varieties of soybean. *Allergy: European Journal of Allergy and Clinical Immunology* 58(12), 1293–1298.

Foucard and Malmheden Yman (1999). A study on severe food reactions in Sweden – is soy protein an underestimated cause of food anaphylaxis? *Allergy: European Journal of Allergy and Clinical Immunology* 54(3), 261–265.

Heine et al. (2006). Proposal for a standardized interpretation of the atopy patch test in children with atopic dermatitis and suspected food allergy. *Pediatric Allergy and Immunology* 17(3), 213–217.

Ballmer-Weber et al. (2007). Clinical characteristics of soybean allergy in Europe: a double-blind, placebo-controlled food challenge study. *Journal of Allergy and Clinical Immunology* 119(6), 1489–1496.

Peanut allergy

Chung and Champagne (1999). Allergenicity of Maillard reaction products from peanut proteins. *Journal of Agricultural and Food Chemistry* 47(12), 5227–5231.

Hourihane et al. (2005). Does severity of low-dose, double-blind, placebo-controlled food challenges reflect severity of allergic reactions to peanut in the community? *Clinical and Experimental Allergy* 35(9), 1227–1233.

Tariq et al. (1996). Cohort study of peanut and tree nut sensitisation by age of 4 years. *British Medical Journal* 313(7056), 514–517.

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