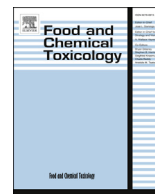




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## Review

# Prioritisation of allergenic foods with respect to public health relevance

## Report from an ILSI Europe Food Allergy Task Force Expert Group.



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## ABSTRACT

Regulators and risk managers in general need to decide whether an allergenic food or ingredient is of such public health importance that it needs to be actively managed. There is therefore a need to scale the relative allergenicity of foods and ingredients according to the hazards they pose. Objective criteria increase transparency and trust in this decision-making process and its conclusions. This paper proposes a framework that allows categorisation and prioritisation of allergenic foods according to their public health importance. The challenge is to find a basis on which the allergenicity of foods can best be described and a method to combine the relevant measures of allergenicity into a scoring system that prioritises allergenic foods on the basis of their public health relevance. The framework is designed in accordance with the generic risk analysis principles used in food safety and can be used by regulators to decide whether or not a specific allergenic food or ingredient is of sufficient public health importance that it warrants regulation (i.e. mandatory labelling) when used in the production of food products.

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## 1. Introduction

Food allergies can result in life-threatening reactions and diminish quality of life. With a prevalence of up to 3% in Europe (Muraro et al., 2014; Nwaru et al., 2014), food allergy is among the most prevalent disorders in the western world. In the past decades the prevalence of food allergies appears to have increased in several regions throughout the world. Although more than 170 foods have been identified as being potentially allergenic (Hefle et al., 1996), a minority of these foods cause the majority of allergic reactions. Some commonly allergenic foods (e.g. milk and eggs) are ubiquitously important on a worldwide basis while other foods most commonly causing allergic reactions vary between geographic regions (Burks et al., 2012). Food allergen labelling legislation currently varies across the globe (Gendel, 2012) but is usually based on the Codex list (Codex Alimentarius, 1999). However, presenting labels which meet consumer needs as well as regulatory requirements has been problematic (Cornelisse-Vermaat et al., 2008), particularly in relation to precautionary labelling to indicate possible unintended allergen presence in food products. Food allergen labelling legislation has not always been based on scientific evidence.

There is a need to scale the relative allergenicity of foods and proteins and the hazards or risks arising from this allergenicity. This includes proteins which pose a known risk to the public and novel proteins arising from biotechnology, modified species or new food sources. Prioritisation according to the public health impact of allergenic foods ensures that scarce resources are allocated in such a way that they address those allergens that matter most from a public health point of view. Both regulators and risk managers in general need to decide whether a food allergen is of such public health importance that it must be actively managed. Objective criteria would improve transparency and trust in the decision-making process and its conclusions.

For the last six years, the ILSI Europe Food Allergy Task Force has developed methods to identify and assess the evidence (schematically represented in Fig. 1). The first peer-reviewed publication focused on scientific criteria for identifying allergenic foods of public health importance (Björkstén et al., 2008). A subsequent publication evaluated their application and further refined them by incorporating an assessment of the strength of available scientific evidence (Van Bilsen et al., 2011). An assessment of the quality of evidence of the scientific literature available as well as an attempt to test the applicability, completeness and ease of use of the

approach suggested in the previous papers was later conducted during a workshop with key stakeholders in September 2010 (Chung et al., 2012).

This paper proposes a framework that would allow categorisation and prioritisation of allergenic foods according to their public health importance. The challenge we address is to propose measurements on the basis of which the allergenicity of foods can best be described and a method to combine the relevant allergenicity measurements into an approach to categorise and prioritise their public health relevance. Once the relevant measurements have been defined, with a clear method of grading them individually, this grading can be used as a basis for ranking allergenic foods relative to each other as threats to public health. Risk managers can then decide on a possible categorisation and prioritisation for risk management purposes. The framework, based on a hazard scaling approach that fits in the risk analysis cycles for food allergens, can be used to decide on labelling advice.

In Section 2, the application of the generic risk analysis cycle to allergenic foods is addressed on the basis of which the most appropriate parameters for scaling allergenicity are selected. Section 3 addresses how these parameters (prevalence and potency) can be used to categorise and prioritise allergenic foods according to their public health relevance and gives examples for such categorisation and prioritisation as a demonstration of principle. The establishment of actual prevalence and potency data to be used for the various allergenic foods and therewith the actual application of the categorisation and prioritisation approach is beyond the scope of this paper and should be subject of future projects. In Section 4 the use of the hazard scaling in categorisation and prioritisation for risk management purposes in the risk analyses process is addressed.

## 2. The risk analysis cycle applied to food allergy and parameters for hazard scaling

The ultimate purpose of the framework we propose is to provide an approach to decide whether or not a specific food or ingredient is of sufficient public health importance due to allergenicity that it warrants regulation (i.e. mandatory labelling) when used in the production of food products. This decision will determine which of more than 170 allergenic foods should be included in the allergenic ingredient labelling requirement for foods to enable allergic consumers to avoid these ingredients.

When introducing a hazard categorisation and risk

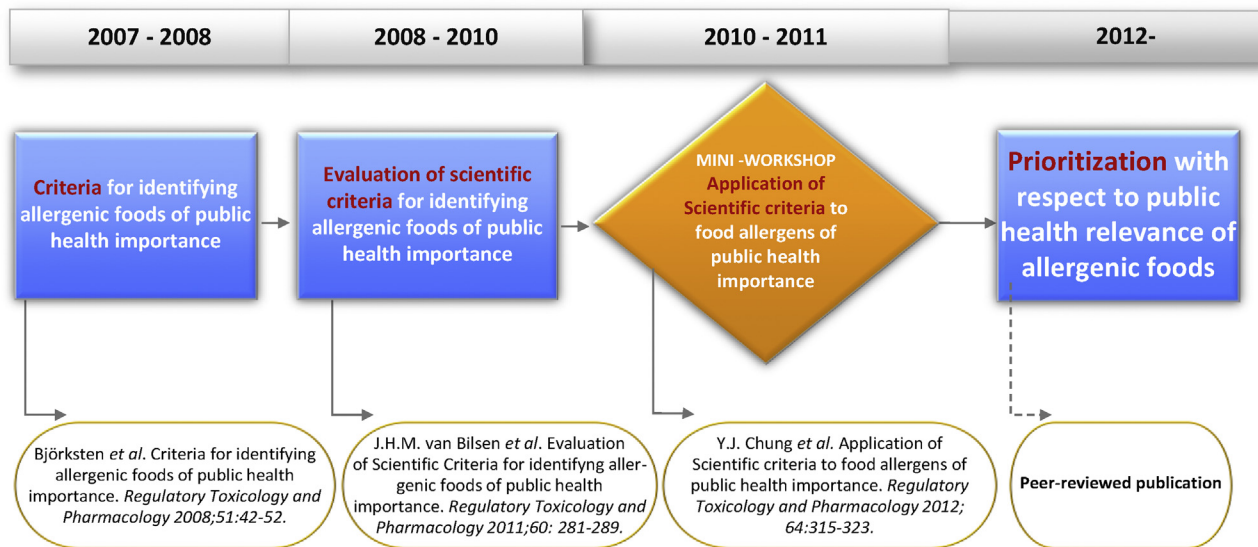


Fig. 1. The journey of the ILSI Europe Food Allergy task force in respect of prioritising allergenic foods according to public health importance.

management approach, it is important to adhere, as far as possible, to existing well established and accepted frameworks. Approaches to food safety have become internationally harmonised during the past decades and generally follow the principles of the risk analysis cycle as published, amongst others, by WHO IPCS (International Programme on Chemical Safety et al., 2004). The chart in Fig. 2 summarises how the classical risk analysis cycle might be applied to the topic of food allergens.

For allergenic foods, two risk analysis cycles can be distinguished. The first is the risk analysis for sensitisation to the allergenic food. This is not the principal subject of the prioritisation tool presented in this paper. The outcomes from the risk analysis for the sensitisation phase (risk as represented by the prevalence of allergy

and the sensitivity of the allergic population for developing allergic reactions upon exposure) are the appropriate “hazard” input for the risk analysis of the elicitation phase, which is the subject of the prioritisation tool presented in this paper. The sensitising potency of an allergenic food together with the degree and pattern of exposure and various other factors determine the prevalence of sensitisation and subsequent allergies in the population and the sensitivity of the allergic individuals, which are developed during the sensitisation phase. The prevalence of food allergies in the population and the sensitivity of the allergic individuals/the potency of the allergenic food for elicitation of reactions, together with the degree and pattern of exposure to the allergenic food and various other factors, determine the frequency and severity of

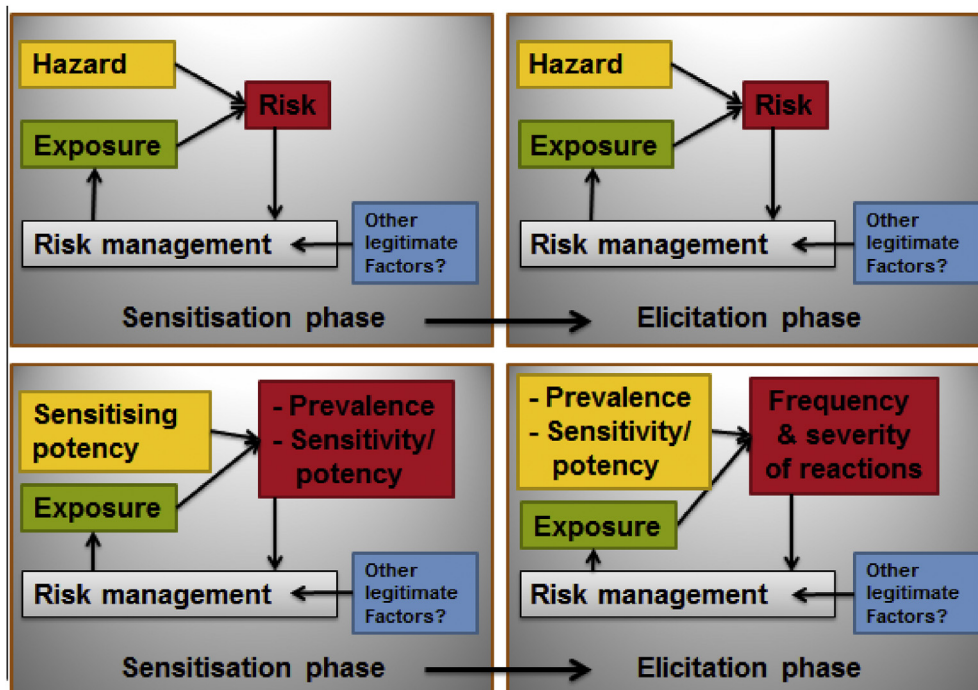


Fig. 2. The generic risk analysis cycle (top) applied to food allergy (bottom).

allergic reactions in allergic individuals, which are developed during the elicitation phase.

Fig. 2 shows that exposure of susceptible individuals to an allergen in the elicitation phase is not an independent determinant. In the elicitation phase, exposure depends on risk management actions, including labelling, that may influence more than anything else, the level of exposure in the allergic subpopulation and thus the frequency and severity of allergic reactions in that population. When there is a low frequency of severe reactions to a certain food, this may indicate good risk management and does not by itself imply that the food should not be a regulated allergen for labelling. Our tool aims at classifying the inherent allergenic properties, regardless of whether they are already well managed in terms of exposure potential, or not. The chart in Fig. 3 explains schematically how exposure to allergens is influenced by the risk management actions already in place and why an assessment of the **inherent properties** of allergens should be independent of the level of exposure that determines the frequency of occurrence of (severe) reactions.

Similar to the exposure element, the severity of allergic reactions as observed in the population is not an independent determinant in an allergen *hazard* ranking exercise. The severity of allergic reactions occurring as a consequence of exposure is influenced by the dose ingested and the potency of the allergen/the sensitivity of the allergic consumer to that allergen. Severity is a component of *risk*, as risk is defined as the function of both the likelihood and the **severity** of an adverse event. Severity of allergic reactions in the population therefore should be taken into consideration in the risk management decision making phase, but should not be part of the allergen specific *hazard* assessment.

Based upon the above reasoning, the expert group concluded that the two independent determinants most appropriate for expressing the potential of allergens to elicit allergic reactions on a population level, are the prevalence of the allergy and the potency of the allergen; the latter being reflected in the distribution of sensitivity of the allergic population to the allergen under assessment. Prevalence and potency can be defined as independent and measurable dimensions: prevalence from the allergic proportion of the population and potency from population threshold dose-distribution curves. The development of a hazard scaling

approach therefore can best be based on these measurements that represent the hazard information in the risk analysis cycle for the elicitation phase.

The parameters and approach for scaling allergenic foods according to their public health importance as proposed in this paper is based on a scaling approach under development by TNO, The Netherlands, in the framework of a programme aimed at developing an approach for predicting and scaling the relative allergenicity of novel or modified food proteins (Houben et al., in preparation). Although the latter approach is mainly focussed on the sensitisation phase and the approach proposed in this paper on the elicitation phase, the two approaches are linked because the outcomes from the risk analysis for the sensitisation phase (i.e. the risk as defined as the chance of and severity of an adverse effect, in the case of sensitisation represented by the prevalence of allergy and sensitivity of the allergic subjects) are the appropriate hazard input for the risk analysis of the elicitation phase (see also Fig. 2).

### 3. Scaling of allergenic foods according to public health relevance

#### 3.1. Evaluation parameters for prevalence and potency

The prevalence of allergy to a specific food is a rather straight forward parameter. We can define this prevalence as the proportion of the population that is allergic to that specific food. Though simple by definition and as such in principle requiring little discussion for use in the hazard scaling approach that we propose, the prevalence of allergies to various foods is not easy to establish and subject to many methodological issues. As this paper aims to present a hazard prioritisation approach and not a methodological discussion on epidemiological issues in establishing the prevalence of food allergies, these issues will not be discussed further and prevalence data used in this paper are to be considered for the purpose of illustrating the hazard scaling approach rather than as actual estimates of prevalence. For a recent overview of food allergy prevalence data, we refer to a report for EFSA (University of Portsmouth (2013)) and the EAACI Food Allergy and Anaphylaxis Guidelines.

The most appropriate expression of potency for use in hazard

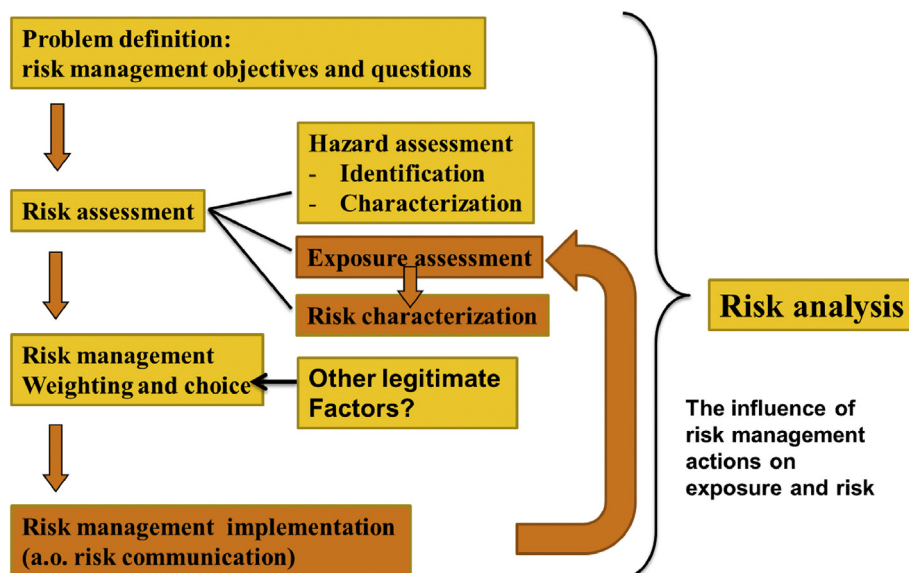


Fig. 3. The influence of risk management actions on exposure and risk.

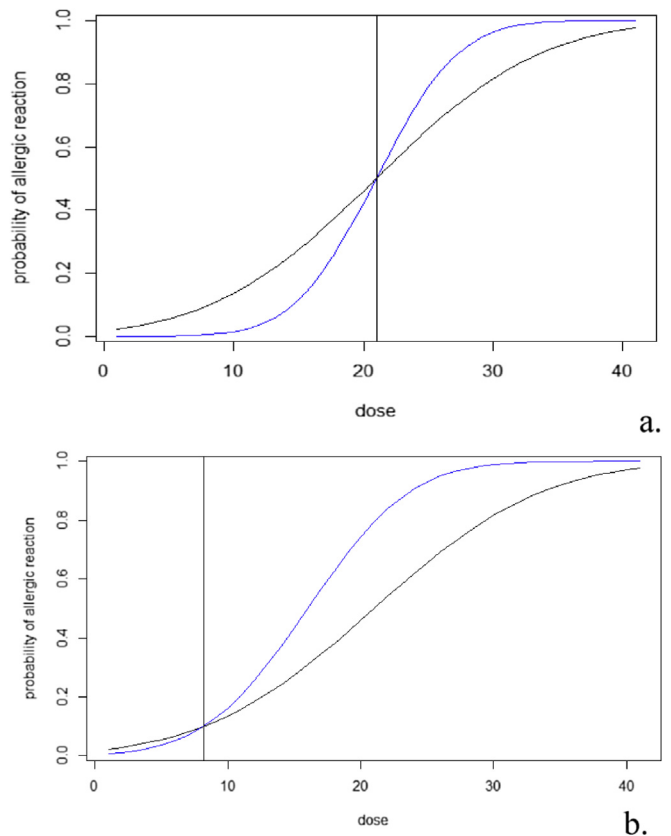


scaling for the elicitation phase is somewhat more difficult to define. There is not just a single potential value for the potency of an allergen for effect elicitation. The potency of an allergen is typically assessed in a clinical setting by means of food challenge studies in which allergic individuals are exposed to increasing amounts of the food to which they are allergic. For each allergic individual participating in such a study, the individual no observed adverse effect level (NOAEL) and lowest observed adverse effect level (LOAEL) are obtained. In theory, no and lowest observed effect levels can be assessed for various (types of) reactions separately, for instance for oral, GI-tract or dermal reactions or the more severe reactions involving the respiratory and/or cardio-vascular system. Some stakeholders may prefer to base a hazard categorisation on the intrinsic potency or capability of allergens to induce severe or more dangerous effects. Such information however is not available as challenge studies generally are terminated prior to reaching doses that induce severe reactions. As explained in the previous section, severity of allergic reactions in daily life is not an independent determinant in an allergen hazard ranking exercise but is a risk term and as such influenced by the level of exposure. The Expert Group therefore proposes to use, as a basis to estimate potency, the distribution of the minimum doses eliciting any type of objective allergic reaction as a basis for hazard scaling, as this will automatically also cover more severe or dangerous types of allergic reactions. The dose eliciting an allergic reaction in 50% or the allergic population (ED50) is proposed as the measure of potency for scaling and comparison between various allergenic foods.

Within the food allergic population there can be substantial variability in sensitivity between individuals, (Taylor et al., 2009; Wensing et al., 2002a,b). A threshold dose-distribution for the allergic population of a specific food can be constructed describing the cumulative proportion of the population reacting to an increasing dose of an allergenic food, the latter usually expressed on a milligram (mg)-protein scale. For the purpose of scaling allergenic foods with respect to potency, we need to derive a useful summary statistic from this threshold dose-distribution that has the following properties: 1) It should reflect potency, i.e., be a valid measure. 2) It should be easy to interpret. 3) It should capture the variability between foods and distinguish sufficiently between allergenic foods in order to scale them. Robustness of the estimate is a concern, since the number of observations and quality of challenge studies varies considerably between food products (for example, for peanut many more individuals have participated in challenge studies than for shrimp).

An obvious choice as a summarizing statistic would be the median of the threshold distribution, often denoted as the ED50, the dose at which 50% of the allergic population will show objective symptoms. It fits the mentioned criteria: 1) The ED50 captures the location of the threshold distribution on the mg-protein scale and as such is a valid measure of potency. The median is also known as a robust statistic that is not as sensitive to outliers as, for example, the mean. 2) The ED50 is easy to interpret. 3) In Section 3.3, several examples of scaling of known allergenic foods are given and from these examples it appears that the ED50 does vary between allergenic foods and distinguishes allergenic foods with different potencies sufficiently.

An important question is how to deal with two allergenic foods having the same ED50 but differing in their ED10, ED05, etc. Statistically speaking, should the variance of the threshold distribution be taken into account in the scaling approach? An example of this is shown in Fig. 4 a showing two imaginary threshold curves with the same ED50 (at the intersection with the vertical line) but different values for the ED10 and ED90, in other words, the cumulative probability curves have different slopes. A practical and statistical argument for not taking account of this variance in the threshold



**Fig. 4.** a) Two hypothetical threshold dose-distribution curves with the same ED50 but different slopes; b) Two hypothetical threshold dose-distribution curves with the same ED10 but different ED50.

distribution is that it is difficult to obtain comparable levels of accuracy of estimation for different allergens, due to substantial variability in available sample sizes for the allergenic products. This makes comparisons of the ED10 or ED05 less robust. A methodological reason for focusing solely on the ED50 and ignoring the ED10 and ED90 is that the purpose of the prioritization is to protect the whole allergic population, and not specifically the most sensitive part of the allergic population. For allergenic foods that demonstrate a flatter slope, the allergic population is somewhat more sensitive below the ED50 in comparison with an allergenic food with a steep slope. However, above the ED50, the allergic population is somewhat less sensitive in comparison with an allergenic food with a steep slope. Fig. 4 b gives another example. In this case we consider two hypothetical threshold dose curves with the same ED10 value, but different ED50 values, again due to different slopes. The curve with the steepest slope obviously is from the most potent allergen in terms of effect elicitation, which is clearly reflected by a lower ED50 value, while the ED10 values would not provide this information.

The ED50 thus seems an appropriate parameter for scaling potency and other options are less robust and/or give no additional information. The expert group therefore decided to use the ED50 for objective effects as the parameter for scaling the potency of allergenic foods.

### 3.2. Proposed scaling approach: combining prevalence and potency information

When considering how to combine the two chosen parameters, prevalence and potency, the expert group considered capturing the

“level of allergenicity” into one single value and scale. However, there are no first-principles from which to derive a single scale or score. Any derivation of a single representative value would imply a relative weighting of each of the two scores for prevalence and potency. In the absence of criteria on which to base such a weighting, the Expert Group considered it best not to combine the parameters but to express them graphically, keeping the detail of the two independent dimensions. In paragraph 3.3, various examples of scaling of allergenic foods are given as a proof of concept illustration of the hazard scaling approach. This graphical representation of the hazard characteristics, as modelled by their prevalence and potency, can then serve as the basis for categorisation and/or prioritisation. The resulting position of individual foods in the 2-dimensional plot relative to each other can be used by risk managers for risk management decision making. Various options of how to use the information in risk management exist, for instance by drawing borders of categorisation between allergenic foods of low or high public health relevance. In Section 4, the use of the hazard scaling in categorisation and prioritisation for risk management purposes in allergen risk analyses is addressed.

### 3.3. Examples of scaling as a proof of concept illustration of the hazard scaling approach

In this paragraph, prevalence and potency data for several allergenic foods are used to present some examples as a proof of concept illustration of the hazard scaling approach. Data on allergenic foods covering a wide range of estimates of prevalence and potency were selected to obtain examples that illustrate how differences in allergenicity (prevalence and potency) and data availability and quality can be captured in a graphical scaling. The selection of allergenic foods and studies or data points therefore was based on capturing:

- differences in prevalence and potency.
- differences in amount of available data points.
- differences in data quality.

In view of the selective data choices specifically aimed at capturing such differences, prevalence and potency data used in this paragraph are not to be considered as actual estimates of prevalence or potencies of the allergenic foods selected but are only meant for illustrative purposes.

For prevalence, several studies from a report for EFSA were selected. For potency, ED50 values derived from the TNO-FARRP Threshold Data Base that was also used for the elaboration of Reference Doses in the framework of the development of the VITAL 2.0 approach (Allen et al., 2009; Taylor et al., 2014) were used. In Table 1, the allergenic foods and data points selected for proof of concept illustration are listed. Fig. 5 gives a proof of concept illustration of scaling of allergenic foods according to their public health relevance in effect elicitation based on these allergenic foods and data points selected.

## 4. Prioritisation of allergenic foods according to public health relevance in the risk analysis process

### 4.1. Hazard categorisation as a basis for risk management decision making

The scaling approach proposed and illustrated as a proof of concept in section 3 can be used for risk management decision making. The ultimate choice of how to use the hazard information in risk management is up to regulators. The approach could be a basis for deciding whether or not to include certain allergenic

foods or ingredients in the labelling legislation. This could be done by drawing a boundary in a graph such as in Fig. 5 between the prevalence and potency combinations that would represent allergenic foods of high and low hazard. Once filled with consensus data on prevalence and potency for the allergenic foods or ingredients, this could be the basis for allocation of these foods and ingredients to a category of allergenic foods of either low or high public health importance. The approach would also allow the amount and quality of data on prevalence and potency to be taken into consideration and decisions could be postponed if data were not considered sufficient for decision making, or made on a conditional basis if a more precautionary stance is deemed appropriate. Lack of sufficient appropriate data might be used to influence research priorities. Based upon the position in the two dimensional chart, and the amount and quality of available data that underpin the prevalence and potency assessment, one can divide the outcome of the assessment of the allergenic foods into different decision categories, purely based on the hazard assessment:

1. Allergens of high public health relevance, based on their prevalence/potency position, stemming from a strong set of data -> advice to label.
2. Allergens of low public health relevance, based on their prevalence/potency position, stemming from a strong set of data -> advice not to label.
3. Allergens for which only a limited data set and/or data of low quality are available -> allergens put “on hold” from a hazard assessment point of view but subcategorised according to high or low priority research needs depending on the potential public health relevance suggested by data available. In general, no change in management regime would be expected until additional data of sufficient quality would indicate another decision, although other legitimate factors could drive a deviation from this principle.

This would result in 4 distinct hazard characterisation categories as illustrated in Table 2.

With the data generated by the hazard classification approach proposed in Table 2, risk managers can make risk management decisions and/or perform risk management interventions. In the case of large amounts and good quality data supporting the allocation of allergens to either high or low health relevance, the risk management decision to be taken may be quite straightforward. For allergens having ended up in the categories “on hold”, additional research may be needed.

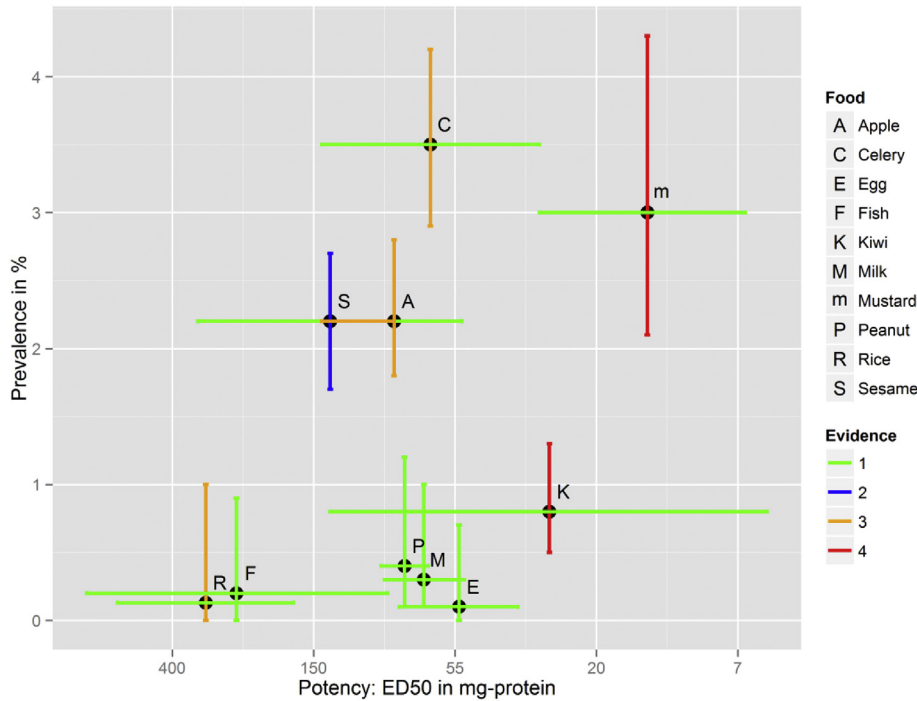
We illustrate the approach for cases with limited data availability by means of three unregulated allergens that were included in the examples in Table 1 and Fig. 5: kiwi, rice and apple. The location of a set of well-known allergenic foods on the allergenicity scale gives a frame of reference for assessing new allergens. The prevalence and potency data used are only meant for demonstration of principle and not as actual prevalence and potency estimates. However, if the data used in Table 1 and Fig. 5 were the actual established consensus data for these allergens, the kiwi, rice and apple cases could be assessed as outlined in the case descriptions below.

For illustrating the assessment in the case studies, a cut off for allocating an allergenic food to the category of allergenic foods of either low or high public health importance is needed as a reference. For this illustration, an established cut off as illustrated in Fig. 6 is assumed. The actual establishment of this cut off as well as how to deal with allergens for which a 95% Confidence Interval (CI) crosses the established boundary (as is the case for fish and kiwi in the example of Fig. 6), is a risk management responsibility.

**Table 1**  
Allergenic foods and data points selected for proof of concept illustration.

Allergenic food	Potency ED50, in mg protein (95% CI)	Data level of evidence (*)	#Threshold data points	Prevalence % (95% CI)	Data level of evidence (*)	Remarks
Egg	53 (35–81)	1	180	0.1 (0–0.7)	1	(Osterballe et al., 2005) n = 936, age > 22, DBPCFC
Fish	256 (88–738)	1	19	0.2 (0–0.9)	1	(Osterballe et al., 2005) n = 936, age > 22, DBPCFC
Sesame	132 (52–336)	1	21	2.2 (1.7–2.7)	2	(Zuberbier et al., 2004)
Mustard	14 (7–30)	1	33	3 (2.1–4.3)	4	(Touraine et al., 2002)
Milk	68 (51–90)	1	351	0.3 (0.1–1.0)	1	Prevalence is self-reported, France only (Osterballe et al., 2005) n = 936, age > 22, DBPCFC
Peanut	78 (66–92)	1	751	0.4 (0.1–1.2)	1	(Osterballe et al., 2005) n = 936, age > 22, DBPCFC
Celery	65 (30–140)	1	39	3.5 (2.9–4.2)	2/3	(Zuberbier et al., 2004) (SPT)
Apple	84 (84–140 gr)	2–4	2	2.2 (1.8–2.8)	2/3	(Zuberbier et al., 2004) (SPT)
Kiwi	29 (6–132)	1	14	0.8 (0.5–1.3)	4	(Rance et al., 2005)
Rice	318 (170–594)	1	13	0.13 (0–1)	3	Self-reported, n = 2716 (Eriksson et al., 2004)

(\*) (Van Bilsen et al., 2011).



**Fig. 5.** Proof of concept illustration of scaling of allergenic foods according to their public health relevance in effect elicitation (Evidence = quality level of evidence: 1 = highest, 4 = lowest quality); (Van Bilsen et al., 2011). For details regarding data, see Table 1.

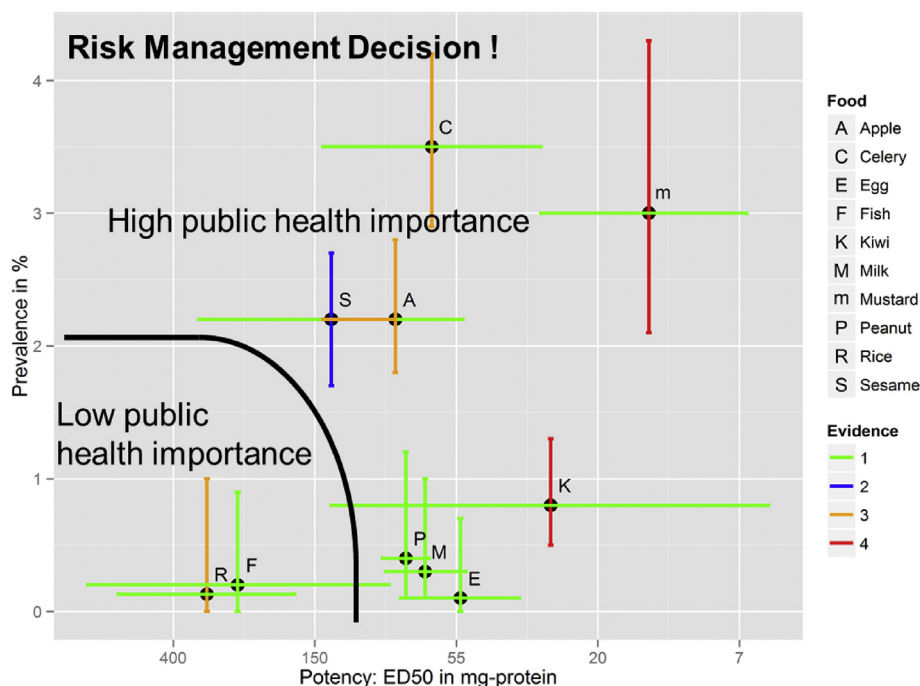
**Table 2**  
Hazard characterisation categories for allergenic foods and ingredients based on assessed public health relevance and data quality and availability.

Quality and availability of evidence			
Public Health Importance (based on potency and prevalence information)			
High	High	High public health importance	Low
		Well established	Potentially high public health importance
		Well established	“On hold”; research needed
		Labelling required	High priority research
Low	Low	Low public health importance	Likely low public health importance
		Well established	“On hold”; research needed
		No labelling required	Low priority research

4.1.1. Case 1 – apple

The potency data for apple was from two patients who underwent a food challenge but of a lower data quality level than a

DBPCFC. The resulting estimate for the potency of apple was 30 g of apple, with a range of 30–50 g, corresponding to 84–140 mg protein. Prevalence data gave an estimate of the prevalence of apple



**Fig. 6.** Illustration of a possible risk management choice for cut-off between allergenic foods of low and high public health importance. For details regarding scaling and data selection, see paragraph 3.3, Table 1 and Fig. 5.

allergy of 2.2% (95CI 1.8–2.8). The prevalence data was of level 3 quality as the best evidence was based on self-reports and the skin prick test. In conclusion, the quality of evidence for apple can be considered low for both potency and prevalence, but the reported potency and suggested prevalence are comparable to other regulated allergenic foods (see Fig. 5 and Table 1). Therefore, the derived conclusion may be that apple is likely to be an allergenic food of high public health importance, that research is needed and that this is of high priority. It should be noted that apple allergy may be different from other allergies, for instance because of the well-known instability of the major allergenic protein. This may pose another perspective with respect to the risks due to cross contamination of food products with apple proteins. Such aspect may be taken into consideration in the ultimate risk management decision making.

#### 4.1.2. Case 2 – kiwi

The potency estimate for kiwi was based on DBPCFC data (14 patients) and thus of high data quality. The ED50 was estimated at 29 mg protein (95CI 6–132), which indicates a relatively highly potent allergenic food, being more potent than peanut or milk and only less potent than mustard. The prevalence was estimated at 0.8% (0.5–1.3), but based on self-reports and thus of low data quality. Therefore, we conclude in this case that kiwi is likely to be an allergenic food of high public health importance, mainly because of the estimated high potency, and more research is needed with a relatively high priority.

#### 4.1.3. Case 3 – rice

The potency estimate for rice was based on DBPCFC data (13 patients) and thus of high data quality. The ED50 was estimated at 318 mg protein (95CI 170–594), which indicates a low to moderately potent allergen, comparable to, for instance, fish. Prevalence data provided an estimate for the prevalence of rice allergy in individuals allergic to other foods. The resulting estimate for the prevalence of rice allergy was only 0.13%. A confidence interval is

not available, since the original estimate did not provide this. Therefore, we conclude that rice, given its low to moderate potency and its low estimated prevalence, is likely to be of low public health importance. More research is needed but this is of low priority.

#### 4.2. Other factors influencing risk management decision making

Risk management decisions can be based solely on hazard information, but as illustrated in Fig. 2, risk management decisions may also take into consideration the frequency and/or level of exposure and/or the consequential frequency and/or severity of effects in the population (i.e. the risk) and/or other legitimate factors. Other legitimate factors often are associated with the impact of the risk management options. Several of these possible factors are briefly discussed below. In principle, some of these factors could be taken into consideration in the hazard categorization method proposed in this paper, provided that relevant prevalence and potency data for the processed food ingredients are available. An example is the potential loss of allergenicity of proteins or loss of allergenic proteins during processing. However, as such considerations may be process or processed food product specific and may not be generic for the original allergenic food, it is preferable to separate the use of such information in the risk management decision making from the hazard categorization of the original allergenic food. For example, loss of allergenic proteins during the production of a highly refined vegetable oil might be a reason for exempting such oil from labeling requirement (risk management decision) but does not make the original allergenic food (e.g. peanut) of low public health importance (hazard categorization of the original allergenic food) requiring no or low risk management priority.

##### 4.2.1. Avoidability, visibility and ascertainability

Many aspects of an allergic food may relate to its visibility, including its suitability for being an ingredient in prepared foods and its allergenic stability when prepared for consumption by



cooking and/or heating. All other things being equal, readily visible allergenic foods are less likely to require control than allergenic foods which are easily and commonly “hidden” in prepared foods.

#### 4.2.2. Reputation and image

Foods may become fashionable or unfashionable because of numerous actual or perceived benefits or drawbacks. While this may affect the prevalence of consumption and frequency of allergic reactions, they may also affect societal demand for control. Certain allergenic foods may also have a “bad reputation” amongst patients and the general public as being a relatively frequent cause of particularly severe or fatal reactions, such as peanut (see below).

#### 4.2.3. Effects on quality of life

Measurements of health related quality of life (HRQL) in food allergy are relatively new. Among the first instruments developed for this purpose were those of the EuroPrevall project. While these instruments have proven valid and useful for measuring HRQL in different food allergic populations and settings, only a few studies have included analyses of differences in the degree of HRQL impairment in patients allergic to different foods.

DunnGalvin et al. (2008) found that peanut allergy was associated with poorer HRQL than other forms of food allergy. This could not be confirmed in a subsequent study where most children were peanut allergic, so that a clear conclusion could not be reached (Wassenberg et al., 2012). In a recent analysis of data from the EuroPrevall study, multiple linear regression analyses were performed to develop models for predicting HRQL in children and adults from different European countries (Saleh-Langenberg et al., 2015). These results show that wheat and fish allergies were associated with poor quality of life in adults, whereas peanut and soy allergies were associated with poor quality of life in children.

While there is currently little information of health related quality of life (HRQL) differences between allergenic foods, the content of HRQL instruments show important domains of patient experience which are likely to make certain allergenic foods more important to allergic individuals than others. These include foods that are relatively important adjunct to social interactions, particularly those where there is some inherent uncertainty about the stringency of avoidance during preparation. Allergenic foods which are served at parties, in restaurants or at other social gatherings might thus be more likely to require control than allergenic foods where this is of less relevance.

#### 4.3. Initiation of a risk analysis process and risk management decision making

A risk analysis process leading to risk management decision making generally will not be executed spontaneously. Changing societal or legislative situations, routine updates or re-assessments or identified or suspected changing or emerging risks may trigger the start of such a process. As the approach using potency and prevalence as the discriminating factors for categorizing foods or ingredients according to the public health relevance of allergenicity is going to generate a snapshot at a given point in time, it is going to be worth adopting an approach capable of keeping track of the continued relevance of an established ranking over time, and able to identify when an update of the analysis is required. Aside from new scientific information, several factors may necessitate the reconsideration of a ranking of public health relevance. The expert group considered these factors, and clustered them under the term “horizon scanning”, to express the idea that an ongoing monitoring activity could provide an alert that an update of the public health relevance assessment may be needed. The expert group assessed both the scope of such horizon scanning, as well as parameters and

sources of information that could be of relevance. Horizon scanning could play a double role, at two different stages of the overall risk analysis process of allergenic foods:

1. First of all, horizon scanning could inform the initial hazard analysis, by scanning scientific information for relevant new data on potency and prevalence of already previously assessed and ranked allergenic foods. It could also scan relevant sources of information for the occurrence of newly emerging allergens, for the increase of incidence of allergies which were previously deemed less common or for identifying discrepancies between conclusions from previous assessments and new data. In this role, horizon scanning could not only provide a trigger for updating a hazard assessment of a previously ranked allergenic food, but could also trigger to assess a previously unassessed, newly emerging allergen.
2. Secondly, horizon scanning could provide input on other legitimate factors, which could be used by risk managers, in order to take their decisions on which of the allergenic foods or ingredients might require prioritized risk management actions, such as labelling obligation, and which foods or ingredients do not.

Based upon these two roles of horizon scanning, the expert group compiled a list of examples of measurements and information sources that might be relevant for horizon scanning (see Table 3). They remarked that, establishing the role of horizon scanning, with the appropriate factors and scope, also renders horizon scanning capable of capturing for instance possible geographical differences in public health relevance of allergens.

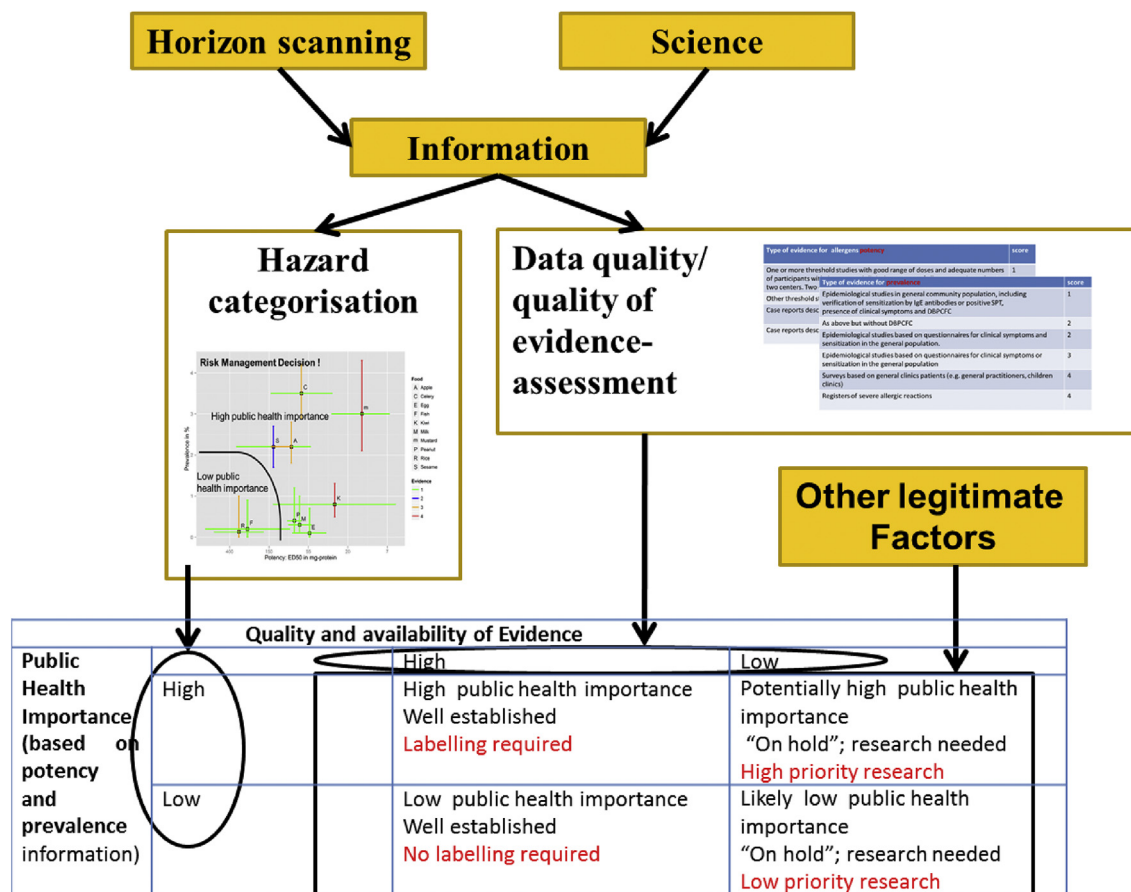
#### 4.4. The overall risk analysis process

As described in the previous sections, the expert group proposes a hazard categorisation approach for prioritising allergenic foods or ingredients according to their public health relevance, based on 2 hazard parameters, i.e. potency and prevalence, as a step in the risk analysis cycle to be applied for binary decision making: should an allergenic food or ingredient be subjected to obligatory labelling as an allergenic ingredient or not. The approach can be applied to any food or ingredient. For some foods or ingredients, sufficient data of good quality will be available for applying the hazard categorisation approach. In such cases the food or ingredient can be categorised either as a food with a well-established high public health importance that should be labelled when used as an ingredient or as a food with a well-established low public health importance for which it has been agreed that no labelling is required. For other foods or ingredients, insufficient data or data of insufficient quality may be available for categorisation. Based on the data available, such foods or ingredients may be classified as potentially being of high or low public health importance, indicating respectively high or low priority research needs. No change in management regime would be expected until additional data of sufficient quality would indicate another decision to be made. The cut-offs for allocation to different hazard categories will need to be decided and agreed on by risk managers. Various other legitimate factors may influence the ultimate risk management decision making. The risk analysis process that results in the risk management decision may be executed as a result of various triggers and reasons that in part may be picked up by continuous scanning for new or changing situations or information for which horizon scanning could be of help.

All risk analysis elements proposed above can be combined in an overall framework/flow chart for risk management decision making in establishing allergenic foods or ingredients for inclusion in the labelling requirement (Fig. 7).

**Table 3**  
Examples of parameters and information sources that might be relevant for horizon scanning.

Source of information	Type of info looked for	Examples
Scientific literature Case reports, Allergen registries Information collected by industry Adverse events reporting trends to authorities	New information on potency and prevalence of food allergens Increase of case reports over time, for a given food allergen Increase in consumer complaints linked to a certain food allergen Increase in reported cases/complaints	Allergen– Centre Charité  CAERS (Consumer adverse event reporting system, FDA) EU authorities and local member states reporting
Screening systems for (changing) dietary intake profiles in a given geography Trends reported by already existing screening tools	Trends in the reporting of incidents, related to food allergens currently not on the EU allergens list National food surveys Changes in Eurostat data on traded foods and imports Authorities screening tools on food incidents Commercial tools	RASSF TNO Emerging Risk Identification Support Foods notified under the novel foods legislation
The notification of new foods to be introduced in a certain geography	Potential concerns related to the Novel Food criteria: <ul style="list-style-type: none"> <li>• Foods and food ingredients with a new or intentionally modified primary molecular structure;</li> <li>• Foods and food ingredients consisting of/ or isolated from micro-organisms, fungi or algae</li> <li>• Foods and food ingredients consisting of/ or isolated from plants and animals, except when obtained by traditional propagating or breeding practices.</li> <li>• Foods and food ingredients to which has been applied a production process not currently used, where that process gives rise to significant changes in the composition or structure of the food or ingredient</li> </ul>	



**Fig. 7.** Framework/flow chart for risk management decision making in establishing allergenic foods or ingredients for inclusion in the labelling requirement.

**Conflicts of interest**

This work was conducted by an expert group of the European branch of the International Life Sciences Institute (ILSI Europe). The expert group received funding from the ILSI Europe Food Allergy Task Force. Industry members of this task force are listed on the ILSI

Europe website at [www.ilsieurope.eu](http://www.ilsieurope.eu).

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### Transparency document

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