# Novel developments in the risk assessment of food allergens

*Geert Houben* and Marty Blom*

TNO, PO Box 360, 3700AJ Zeist, The Netherlands; Geert.houben@tno.nl

## Abstract

Risk assessment of food allergens has made an enormous development during the last decade. Depending on the risk management question and goal, different approaches can be followed in risk assessment, which is also the case in food allergen risk assessment. Particular for population risk management purposes, probabilistic quantitative risk assessment is nowadays considered the most appropriate approach. Probabilistic quantitative risk assessment was first proposed and developed for food allergen risk assessment by TNO, The Netherlands, and has been used in the development of the current Voluntary Incidental Trace Allergen Labeling (VITAL® 2.0) guidance of the Australian-New Zealand Allergen Bureau and for the quantification of risks of (possible) unintended allergen presence in food products. The approach provides many advantages over other approaches and many different applications are possible, like for instance to assess and compare the efficacy of various management options in reducing the risks of allergens in food chains. However, the approach also depends on stakeholders' ability to deal with risks. In this paper, some background on the need for and principle of probabilistic risk assessment in food allergy as well as some examples of its application and interpretation are discussed.

## Introduction

Food allergy is an adverse reaction to food component in which the immune system is involved. Most food allergies are IgE antibody-mediated in which food proteins are the triggering constituents. IgE-mediated food allergy develops in 2 phases: during the sensitization phase exposure to food proteins causes the production of IgE antibodies and during the elicitation phase renewed exposure to the proteins through food intake triggers allergic reactions. These reactions may be mild but may also be severe systemic reactions that may be fatal. Prevention of the development of food allergy or cure of food allergy are both not yet possible and the main management strategy is the avoidance of allergenic food by food allergic consumers. This, unfortunately, is currently not easy or often even impossible because allergen information on food products is far from clear. Particularly the precautionary warning with respect to potentially unintended allergens present in food products appears to show no or poor correlation with the actual risks associated with unintended allergen presence (Spanjersberg et al. 2010, Remington et al. 2015). The need of probabilistic risk assessment in food allergy originally, and mainly, derives from issues of unintended allergen presence, and that area is also where the assessment finds its main application at this moment.

Probabilistic risk assessment in food allergy

Depending on the risk management question and goal, different approaches can be followed in risk assessment, which is also the case in food allergen risk assessment. A zero risk based approach, as is common in toxicology, may be the top of mind approach for some stakeholders in the case of food allergy. However, a zero risk based approach often results in non-conclusive assessments or impractical conclusions in food allergen risk assessment and therefore is unsuitable for most risk management goals. The application of probabilistic modeling in food allergy risk assessment was first proposed and developed by TNO, The Netherlands (Spanjersberg et al. 2007) and is nowadays considered the most appropriate approach in food allergy risk assessment for population risk management purposes (Madsen et al. 2009). The approach has particularly become broadly applicable following the development of the world largest food allergy threshold database and a food consumption database both specifically attuned to the data requirements for probabilistic risk assessment (Figure 1).

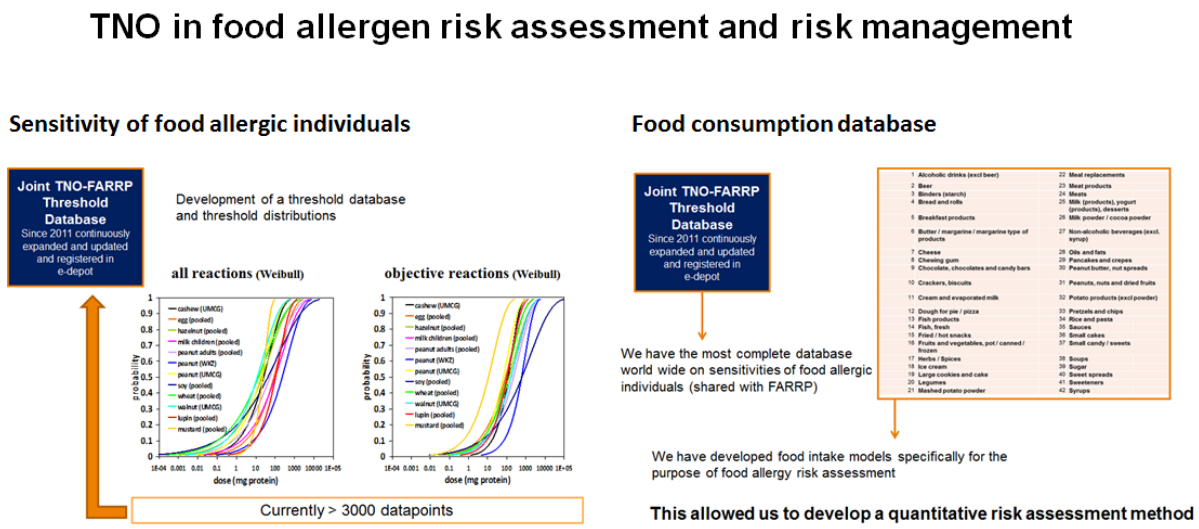


Figure 1: Development of data bases for probabilistic risk assessment in food allergy by TNO

Initially, many questioned whether in food allergy thresholds exist below which allergic responses would not occur. Although we still don't understand how exposure patterns influence sensitization or tolerance inducing processes in food allergy, all stakeholders nowadays agree that thresholds do exists with respect to elicitation of an allergic reaction. Low dose challenge studies have provided insight into dose levels minimally required to elicit allergic reactions in individual patients and into the distribution of these minimal eliciting doses among the allergic population. Threshold data and population threshold distribution curves are now available for many of the major allergenic foods (Figure 1).

Together with information on the levels of an allergen in food products, data from the threshold and food consumption databases are the main input parameters for probabilistic modeling in food allergy risk assessment (Spanjersberg et al. 2007). Depending on the risk

management question, the output from the risk assessment can be expressed in various ways, for instance, as the chance of an allergic reaction when a food allergic individual eats a food product with a certain level of allergen in it. Examples of such risk quantification can be found in for instance Spanjersberg et al. 2010, Remington et al. 2015.

Besides the advantage of having the best state of the art quantification of risks, probabilistic quantitative risk assessment provides excellent opportunities to get insight into the uncertainties in risk assessment and the contribution of the various elements (e.g. estimation of level of contamination of a food product with an allergen, the assumed food intake, or knowledge on the sensitivity of the allergic population) to the uncertainties. Probabilistic quantitative risk assessment can also be used to assess and compare the efficacy of various management options in reducing the risks of allergens in food chains. Databases and methodologies for probabilistic quantitative risk assessment will continuously be further developed and uncertainties in the assessments will decrease over time, but stakeholders generally agree that the approach is ready to be applied for most major food allergens.

The use of probabilistic principles in deriving action levels for precautionary labeling

Probabilistic principles can also be used in the development of action levels for precautionary labeling of unintended allergen presence. A well-known example is the Voluntary Incidental Trace Allergen Labeling (VITAL® 2.0) approach developed by the Australian-New Zealand Allergen Bureau, with support of the VITAL Scientific Expert Panel (Taylor et al. 2014, Allen et al. 2014). The VITAL® 2.0 approach is based on a consensus among stakeholders regarding the desired food safety objective: “What is the risk level that should trigger risk mitigation measures or precautionary allergen labeling in case further risk mitigation is not feasible and what range of residual risks is considered acceptable and should not lead to a precautionary statement?”. This agreed safety objective is used as the starting point for a process of calculation of action levels (Figure 2). This approach is now increasingly being used by food companies and authorities.

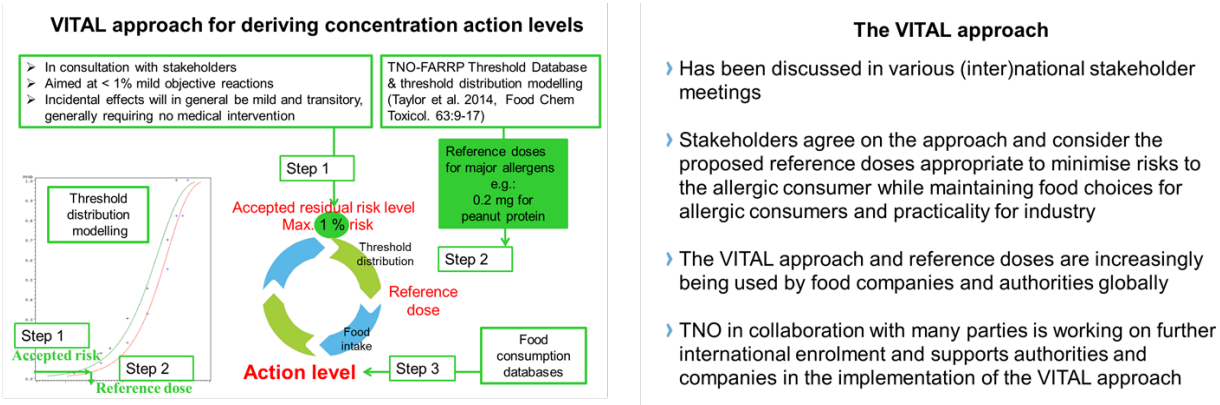


Figure 2: Development and application of the VITAL® 2.0 approach (Australian-New Zealand Allergen Bureau) http://allergenbureau.net/vital/

Dealing with risks

Currently, the most important issue for the applicability of probabilistic quantitative risk assessment in food allergy is the fact that the approach depends on our ability to deal with risks. A zero risk in food allergy is not feasible and stakeholders need to agree on and accept a chosen balance between reducing risks on the one hand and feasibility, practicability and ensuring food choice for allergic consumers on the other hand. This appeared possible in the development of the VITAL® 2.0 approach in Australian-New Zealand. Stakeholders all over the world agree that this is the way forward, but often struggle with ultimately deciding and dealing with accepting a residual risk. Understanding the impossibility of a zero risk situation is also crucial in the interpretation of results of probabilistic risk modeling in food allergy. Probabilistic modeling will always predict a certain level of risk, as this is inherent to the methodology. Further analyses of the results of probabilistic modeling can help in the interpretation of the results, for instance by showing that a very small percentage of predicted allergic reactions was due to the computer model sampling eliciting dose levels far below the minimal eliciting doses of the most sensitive patients in the database, sampling food intake levels far in excess of food intake levels of extreme users or both. Such insights will indicate that, even though the, model might predict a chance on allergic reactions of for instance 0.3%, the risk prediction was based on unlikely extreme outliers of sensitivity and food consumption and thus reactions are in reality very unlikely to occur.

Concluding remarks

- Hazard and zero risk based approaches in food allergy often lead to non-conclusive assessments or unpractical conclusions and may lead to unlimited efforts to reduce allergen levels, improve analytical sensitivity, prove absence of allergenicity, etc.

- Quantitative risk based approaches can give insight in the magnitude of risks and can be used as a basis for deriving “safe” levels of exposure and required analytical sensitivity

- Risk based approach requires agreement among stakeholders on how to deal with risks (risk perception and risk acceptance) and willingness to take another perspective

References

Allen, K.A., Remington B.C., Baumert J.L., Crevel R,R,W., Houben G.F., Brooke-Taylor S., Kruizinga A.G., Taylor S.L. Allergen reference doses for precautionary labeling (VITAL 2.0): Clinical implications. Journal of Allergy and Clinical Immunology. Journal of Allergy and Clinical Immunology, Volume 133, Issue 1, January 2014, 156-164.

Madsen C, Hattersley S, Buck J, Gendel S, Houben G, Hourihane J, Mackie A, Mills C, Norhede P, Taylor T, Crevel R. Approaches to risk assessment in allergy: Report from a workshop "Developing a framework for assessing the risk from allergenic foods. Food and Chemical Toxicology 47, 2009, 480–489.

Remington B., Baumert J., Blom M., Houben G., Taylor S., Kruizinga A., Unintended allergens in precautionary labelled and unlabelled products pose significant risks to UK allergic consumers. Allergy, 70, 2015, 813–819

Spanjersberg M.Q.I., Knulst A.C., Kruizinga A.G., Van Duijn G., Houben G.F., Concentrations of undeclared allergens in food products can reach levels that are relevant for public health. Food additives and Contaminants, Part A, Volume 27, Issue 2, 2010, 169 – 174.

Spanjersberg M.Q.I., Kruizings A.G., Rennen M.A.J., Houben G.F. Risk assessment and food allergy: the probabilistic model applied to allergens. Food and Chemical Toxicology, 45, 2007, 49-54.

Taylor, S.L., Baumert J.L., Kruizinga A.G., Remington B.C., Crevel R.W.R., Brooke-Taylor S., Allen K.J., The Allergy Bureau of Australia & New Zealand, Houben G.F. Establishment of reference doses for residues of allergenic foods: Report of the VITAL Expert Panel. Food and Chemical Toxicology 63, 2014, 9-17.