# Development and evolution of risk assessment for food allergens

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The risk from the unintentional presence of an allergen in a food product must be assessed before it can be managed effectively. Using probabilistic modelling, the risk can be assessed by combining data on the minimum eliciting doses (MEDs) in the allergic human population with exposure data (consumption and contamination data). This paper, commissioned by the ILSI Europe Food Allergy Task Force and published in the peer-reviewed journal Food and Chemical Toxicology, discusses the strengths and limitations of this approach. It is the second paper in a three-part series.

As outlined in the first paper of this series, the risk posed by the inadvertent presence of an allergen in food products is related to two inputs. The first is the minimum eliciting dose (MED) which is the lowest dose of a food allergen which initiates a reaction in an allergic individual. Individual MEDs can be combined to estimate or model the distribution of MEDs in the allergic population. The second is exposure to the allergen. This has two components, contamination, which is the level of allergen unintentionally present in the food product and intake, which is the amount consumed and the frequency of consumption. As the quality of risk assessments depends to a large extent on the availability and quality of the input data, the strengths and limitations associated with these are outlined below.

Controlled clinical challenge studies enable calculation of MEDs and thereby form the cornerstone of the allergen risk assessment. While this type of study offers a number of advantages, for example no species to species extrapolation and good evaluation of individual variability, it also poses some notable limitations which may impact on the distribution of MEDs in the allergic population and thus the overall risk assessment:

1. The degree to which individuals participating in challenge studies represent the overall allergic population is a source of potential uncertainty. It is common practice in many clinics to exclude from challenge studies individuals with greater sensitivity such as those who report severe anaphylactic reaction. However, more significant is the exclusion of less sensitive individuals who manage their reactions without clinical help. In fact, these individuals may not even be known to the relevant health services. As the latter is more common, estimates of population MED tends to be conservative (i.e. lower rather than higher).
2. A range of factors can affect the MED of an allergic individual on any given day, for example exercise, infection, alcohol usage and medication. To minimise their impact, a protocol for low dose challenge studies has been developed and a consensus has been agreed on various aspects. These are the withholding of certain medications before and during challenge studies, time intervals between doses and fasting periods before challenges. However, not all challenge studies are conducted with this protocol.

3. The outcome of challenge studies can be affected by the form of the challenge material such as ground versus whole peanuts, the type of processing and the fat content.

While the MED is a critical input for assessing the risk posed by the inadvertent presence of an allergen in a food so is exposure to the allergen itself. Accurate exposure assessment plays an important role in the overall risk assessment and a number of variables must be carefully considered.

1. Allergen contamination: To assess the level of contamination in the product of interest, representative sampling must be conducted over time such as over one production batch. However, representative sampling is particularly challenging if the allergen is not evenly distributed throughout the product. Regarding testing methods, immunochemical methods such as Enzyme-Linked Immunosorbent Assays (ELISA) have become the standard. Such methods detect proteins from the allergenic source of interest. They are both sensitive (as they can detect very low levels of allergens) and rapid. However, ELISA methods vary considerably from one commercial method to the next. These variations need to be carefully understood so as to ensure the results are meaningful and can be applied to the risk assessment process.
2. Allergen intake: Food consumption/intake data is generated from national dietary surveys. The underlying purpose behind these surveys is to estimate nutrient intake and understand dietary habits. The structure of dietary surveys reflects these purposes and thus the data is often not optimal for food allergen risk assessments. Furthermore, the structure of dietary surveys can vary between countries and thus although many foods are produced for a pan-European market the allergen risk assessments need to be conducted at a national level.

Combining data on MEDs in the allergic population with exposure data is known as the risk assessment. The authors discuss two main methods: the deterministic approach and probabilistic modelling. The latter is widely acknowledged as the preferred approach because it inherently accounts for variability and uncertainties in the inputs. In practice, the software repeatedly samples the data distribution for each of these inputs. It does this by picking a value from each at random and building a distribution representing the probability of an allergic reaction.

Lastly, the authors considered the risk posed by the combined consumption of food products contaminated with the same allergen and concluded that this poses no significant additional health risk.

## For more information please see:

Crevel RWR, et al. (2014). Part II: Development and evolution of risk assessment for food allergens. Food and Chemical Toxicology 67:262-276