Chapter | six

From Hazard to Risk – Assessing the Risk

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CHAPTER OUTLINE

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INTRODUCTION

It is well described that foods such as milk, egg, peanut, shrimp, etc. constitute a hazard to individuals who are allergic to these foods. To go from hazard (is this dangerous and to whom?) to risk (what is the probability that a sensitive person will meet this food in a sufficient amount to cause a reaction, and how serious will that reaction be?) is a procedure that demands detailed knowledge of levels and frequencies at which allergenic material is present in foods, amounts of food consumed, and data on the doses that elicit allergic reactions of certain types (e.g., oral allergy syndrome, skin effects, etc.) and how this reactivity is distributed in the allergic population. This level of detail is not always available, so it may be necessary to make assessments based on incomplete data. With incomplete data it may not be possible to produce a fully quantitative estimate of the risk, but rather judgment can be made, for instance, about whether the concentration of an allergen is likely to be unsafe or not.

Safety assessment and risk assessment are part of the risk analysis concept, which also includes risk management and risk communication. These elements are separate tasks often performed by different players, but they should be part of an interactive and iterative process [1]. Ideally, the safety assessment or risk assessment of allergenic foods is a purely scientific process that utilizes expertise in food allergy, toxicology, and food intake assessment.

Risk assessment of food allergens differs from most other assessments of food-borne hazards because only a small proportion of the population is at risk. In addition, the allergenic food that may be lethal to consume for the food allergic person is often an important nutrient for the rest of the population.

The attempt to estimate the risk from intake of hazardous chemicals is a classic toxicological discipline that has been in existence for many years. Most

toxicological risk assessments are not able to determine a quantitative risk but establish a level that is judged to be safe, often translated into an acceptable daily intake (ADI). Assessing the risk from contamination with hazardous microorganisms is also a well-recognized discipline, and advanced mathematical modeling has been developed, allowing an actual quantitative estimate of such risk. These probabilistic models are now also used in toxicology. Risk assessment in food allergy relies on the methods developed in toxicology and microbiology. As in the other disciplines, food allergy safety or risk assessment can be conducted using different methods, depending on the scope of the assessment and the data available. In this chapter we will present two safety assessment methods and one risk assessment method in food allergy, with examples of their use [2].

WHY AND WHEN IS IT NECESSARY TO ESTIMATE THE RISK FROM ALLERGENIC FOOD?

For many chemical substances, acceptable or tolerable levels in foods are defined in regulation (e.g., food additives, pesticides, mycotoxins). This means that the public and industrial risk managers can use these regulatory thresholds to decide whether a content or level of contamination is acceptable or not. As the levels are included in the legislation, they can be used and discussed and will be the same in products A and B, and often also the same in countries X and Y.

In contrast, regulatory thresholds for allergenic foods have not yet been developed. Current European, US, and other legislation on allergenic food ingredients define which allergenic foods must always be declared on a product label, regardless of the level of use. Except for Switzerland, this only applies to ingredients deliberately added to a food according to a recipe. This legislation does not set any specific thresholds for labeling of these allergenic foods. In reviews conducted several years ago, regulatory authorities generally concluded that data were inadequate to define safe thresholds for food allergens, although they accepted that such thresholds do exist [3,4]. Most legislation has not directly addressed the issue of allergen cross contamination. While there is some voluntary guidance that includes qualitative advice for industry on how to assess and manage risk from allergenic foods [5], there is currently no advice from regulatory bodies or compliance authorities on levels of allergen cross contamination above which precautionary (advisory) labeling (such as 'May Contain Nuts') should be used.

Because of the current absence of agreed upon defined thresholds, food producers as well as enforcement authorities have to decide what level of allergenic food in a given product constitutes a health risk and therefore requires action to manage and/or communicate the risk. The basis for this decision is a safety or risk assessment.

A safety or risk assessment for an allergenic food can be needed for many different reasons. However, food allergen risk assessment has gained most attention in relation to understanding the risk arising from the unintended

presence of an allergen in a product (e.g., through cross contamination). This refers to situations where allergens are unintentionally present in food products, for instance due to practical issues with cleaning production facilities between production runs (for example, water cannot be used when cleaning chocolate production facilities) or due to residues of raw materials arising at any point in the supply chain (harvest, storage, transport, etc.). This chapter and the examples in it will mainly focus on risk assessment for such cross contamination scenarios. The risk assessment principles and methodologies, however, can be applied generally.

The approaches described are applicable to foods containing allergens in non-particulate distributions and cannot directly be used to assess the risk from sporadic contamination with particles such as whole seeds, pieces of nuts, or clots of dough, for which a different approach will be required. However, the probabilistic approach in risk assessment can also be used to deal with particular contamination scenarios, and this will be addressed in this chapter as well.

SAFETY ASSESSMENT IN FOOD ALLERGY USING ONE DATA POINT (NOAEL OR LOAEL) AND AN ESTIMATED FOOD CONSUMPTION

In traditional toxicological risk assessment approaches, data from animal experiments are typically used. The NOAEL (no observed adverse effect level) is typically divided by an uncertainly factor of 10 to allow for differences in sensitivity between animals and humans, and then divided by another uncertainty factor of 10 to account for inter-individual variation among humans. If the LOAEL (lowest observed adverse effect level) is used instead of the NOAEL, an additional uncertainly factor is applied. An allergic individual's LOAEL is equivalent to their minimal eliciting dose (MED) for an allergic reaction. The terms LOAEL and MED have been used interchangeably in previous texts, but the LOAEL will be used for the remainder of this chapter. In food allergen risk assessment it is neither relevant nor necessary to use data from animal experiments, as human data are available from diagnostic and other clinical food challenges. Furthermore, a reliable and predictive animal model for human allergic reactions to food does not currently exist. The most relevant information used for food allergen risk assessment is threshold data from food allergic individuals who have undergone clinical low dose challenge trials (see chapters 4 and 5). In most instances, individual NOAEL and LOAEL values can be derived from those clinical threshold studies. However, in some challenge trials a small fraction of the allergic patients may experience reactions even at the lowest dose administered, so NOAELs cannot be determined. It is also impossible to say with certainty that the most sensitive food allergic individual has been seen in these low dose challenge trials (or indeed any other food challenge studies).

As the data used in the food allergy assessment are from studies in humans, it is not relevant to use the first uncertainty factor of 10. Depending on the

quality of the study and the inclusion criteria for the patients, it may be relevant to include an uncertainty factor that takes into account the uncertainties arising from the establishment of the NOAEL and the possible exclusion of a sensitive fraction of the allergic population.

The US Food and Drug Administration (FDA) Threshold Working Group outlined one example of how this approach might be used for food allergens [4], but there has been no overall consensus on how NOAEL or LOAEL data from clinical challenge trials, with or without the use of uncertainty factors, should be used in food allergy safety assessment. It is likely that one of the reasons for this is that when using NOAELs or LOAELs and an uncertainty factor of 10 or more, the numbers derived are so low that they are below the level that can be reasonably attained in production of food for normal consumption and below the limit of detection of analytical assays for food allergens – and hence not very useful for risk management. Furthermore, reliance on only one data point (or two if using separate data for adults and children) places heavy emphasis on the quality of study design (e.g., dose spacing) and introduces further uncertainty regarding the degree to which the threshold derived is representative for the whole population in question (more about uncertainty factors on page 20).

Despite the above, NOAELs or LOAELs from challenge studies may be used for an initial first assessment or for *the* assessment if this proves sufficient for a sound decision on the level of risk (e.g., the exposure dose of the allergen would be sufficiently high to pose an allergenic risk for the affected population) or if no more data are available.

Example: Spice Mix with Undeclared Wheat Flour as Carrier

A sauce has 10 g spice mixture/kg as an ingredient. It is found that the spice mixture contains (an unknown amount of) wheat flour as carrier. The wheat flour does not appear on the list of ingredients. The question to the risk assessor is, could the undeclared wheat flour be a risk to people with a wheat allergy?

NOAEL/LOAEL APPROACH

As the amount of wheat flour in the spice mix is unknown, it is assumed that 50% of the spice mix is wheat flour. The protein content of wheat flour is 10%. The serving size of the sauce is estimated to be 150 g. This gives a dose of 75 mg wheat protein per serving. Based on a literature search, the LOAEL for wheat protein in children based on objective symptoms is 2.6 mg wheat protein [6]. The dose of 75 mg wheat protein is significantly higher than the LOAEL for objective symptoms and could present a health risk to individuals with wheat allergy. Additionally, individuals that suffer from celiac disease are at risk from this level of wheat protein. So the simple answer is yes, the undeclared wheat flour can be a risk to people with wheat allergy (as well as those with celiac disease).

The challenge with using the NOAEL/LOAEL approach is that it does not take into consideration the population distribution of wheat allergic individuals,