

# How scientists assess if a food is safe for allergic people

By Pia Nørhede

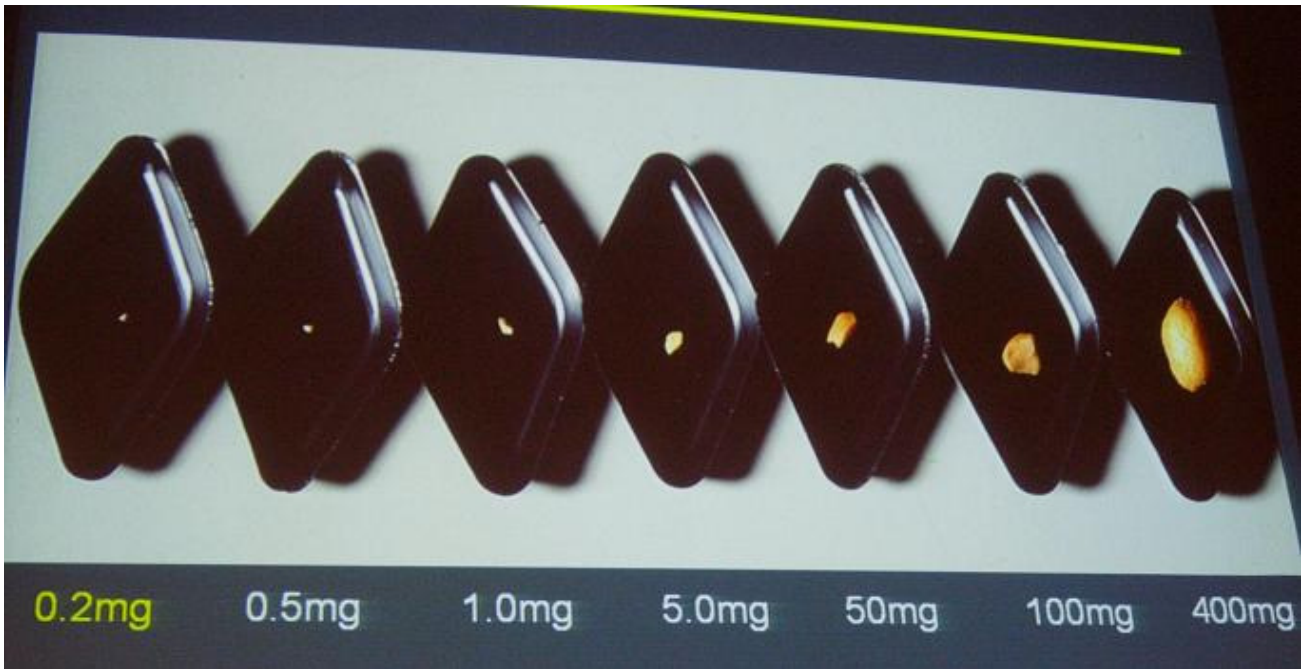
*The law requires food companies to provide safe foods. As a consequence food companies need to find out if their products pose a risk for allergic people. In May 2007 the EU-project EuroPrevall conducted a workshop in cooperation with the UK Food Standards Agency and ILSI Europe. The workshop participants discussed three different ways of using available scientific data to predict if a food product is safe for the majority of allergic individuals. Each approach has weaknesses and strengths. For all of the approaches scientists would like more and better data to be able to predict the safety of a food product with more certainty.*

The law requires food companies to provide safe foods. As a consequence food companies need to find out if their products pose a risk for allergic people. The law has specific labelling requirements for those foods most commonly causing allergic reactions, so that the consumers buying prepacked labelled food should never be in doubt about its composition. For example labels need to indicate clearly that casein comes from milk, and peanut oil may not be hidden under the term vegetable oil. The labelling law does not cover the unintentional presence of allergenic food. Nevertheless food companies need to assess the risk of the unintentional presence of allergenic food in their products in order to decide if it is relevant to warn allergic people of the risk for example by adding a warning such as "May contain traces of nuts".

In practice it is hard to assess how big a risk a food product poses for allergic people, as researchers in food allergy are not yet certain how much of a food is needed to cause an allergic reaction. Recent research has concluded that there exist lower limits of intake below which food allergens will cause only minor or even no apparent symptoms and that these limits vary from one allergic individual to another and even within the same individual at different times. The amount that may trigger allergic reactions observable by others ranges from a tenth of milligram in rare cases, up to grams and sometimes tens of grams, with considerable differences between individuals as well as between allergenic foods. Enough scientific data probably exist worldwide for cows' milk, eggs and peanuts to allow statistical analyses to predict doses of those foods safe to eat for the majority of allergic individuals. However, scientists and regulatory authorities have only recently started to discuss how to make statistical evaluations of the data.

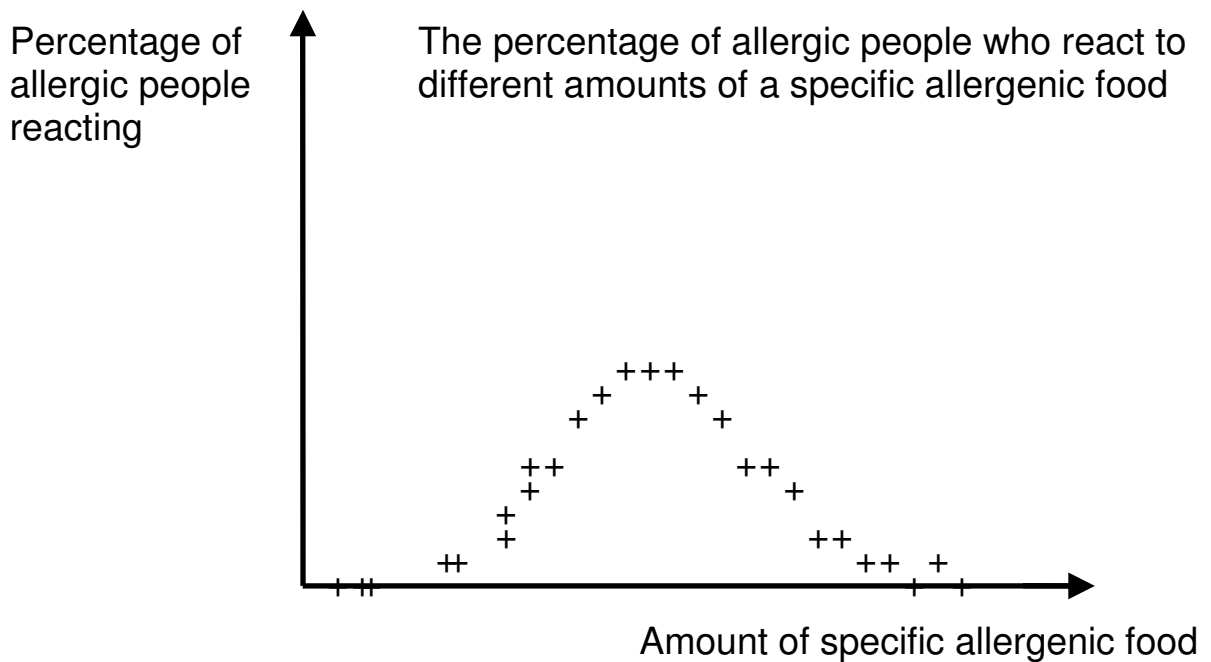
## **How scientists obtain data on the lowest doses of food able to provoke allergic reactions**

Allergy specialists use food challenge tests to find out whether someone is allergic to a food and have adapted these tests to find out the lowest amount that can provoke a reaction in a person at a certain time under certain conditions. A challenge test involves giving a patient increasing doses of the suspected allergenic food, allowing ample time (usually 15 to 30 minutes) between doses for a response to occur. For older children and adults, challenges are normally conducted in a double-blind manner with the suspected food disguised in a special recipe. The recipe without the suspected food is usually given on a separate day and is called the placebo control. Clinicians refer to this diagnostic method as a double blind, placebo-controlled food challenge (**DBPCFC**). This is when neither the patient, nor the investigator knows whether or not the food preparation being given contains the specific allergenic food under investigation hidden in it.



Increasing amounts of peanut as used in a challenge test

When a DBPCFC is used to diagnose food allergy, the aim is to confirm whether a patient has an allergy or not. In practice, many of the patients who had this type of test suffered an allergic reaction when they ate the first dose of the suspected allergenic food. In those cases, the minimum amount able to trigger a reaction was clearly not found. In the last few years, doctors have started challenge tests with tiny amounts of allergenic food (as low as a few millionths of a gram) and they have therefore been able to detect in almost all cases the lowest amounts to which those patients might react. They have also been able to see how many people reacted to different amounts of allergenic food and so build up a picture of the proportion of people tested who react to measured amounts of allergenic food.



## The three different approaches to assess if a food is safe for allergic people

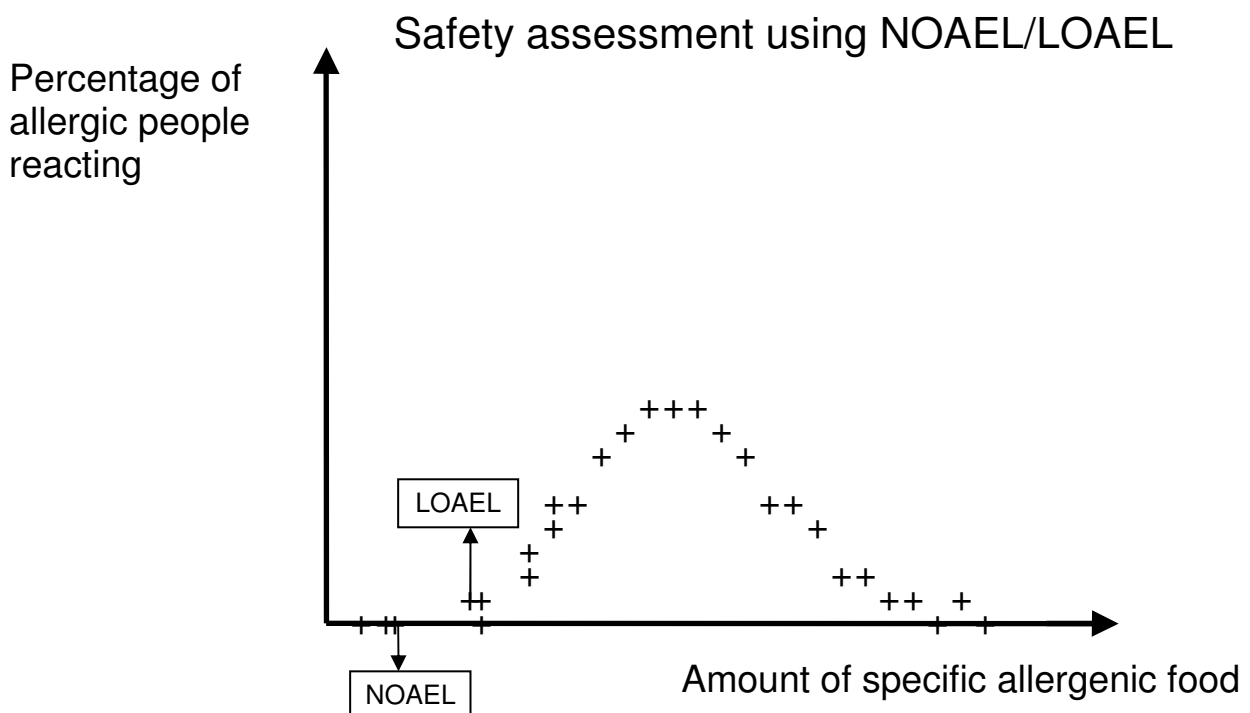
In May 2007 the EU-project EuroPrevall conducted a workshop in cooperation with the UK Food Standards Agency and ILSI Europe. The workshop participants from several governments, universities, research institutes, allergy clinics, patient organisations, and the food industry discussed three different ways which could be used for available DBPCFC data to predict if a food product is safe for the majority of allergic individuals:

1. Safety assessment using NOAEL/LOAEL
2. Safety assessment using Benchmark Dose
3. Risk assessment using probabilistic models

All three approaches use scientific data to predict how safe the food product is or how many people are at risk for an allergic reaction. This safety or risk assessment is a pure scientific process. However, all stakeholders (for example allergic patients, the food industry, scientists, health professionals, and national food authorities) need to discuss and decide when a food product is safe enough or what an acceptable risk is. This is called risk management and was not discussed at the workshop.

### *Safety assessment using NOAEL/LOAEL*

This is the simplest approach. Scientists do not need to know or use any statistical models. From the available DBPCFC data they identify the **NOAEL** (No Observed Adverse Effect Level) or the **LOAEL** (Lowest Observed Adverse Effect Level), if lack of data makes it impossible to identify the NOAEL for a specific allergenic food. As you can see in the figure below, the NOAEL is the highest amount of allergenic food, which in DBPCFCs has not caused any allergic people to react. The LOAEL is the lowest amount of allergenic food where some allergic people have reacted.



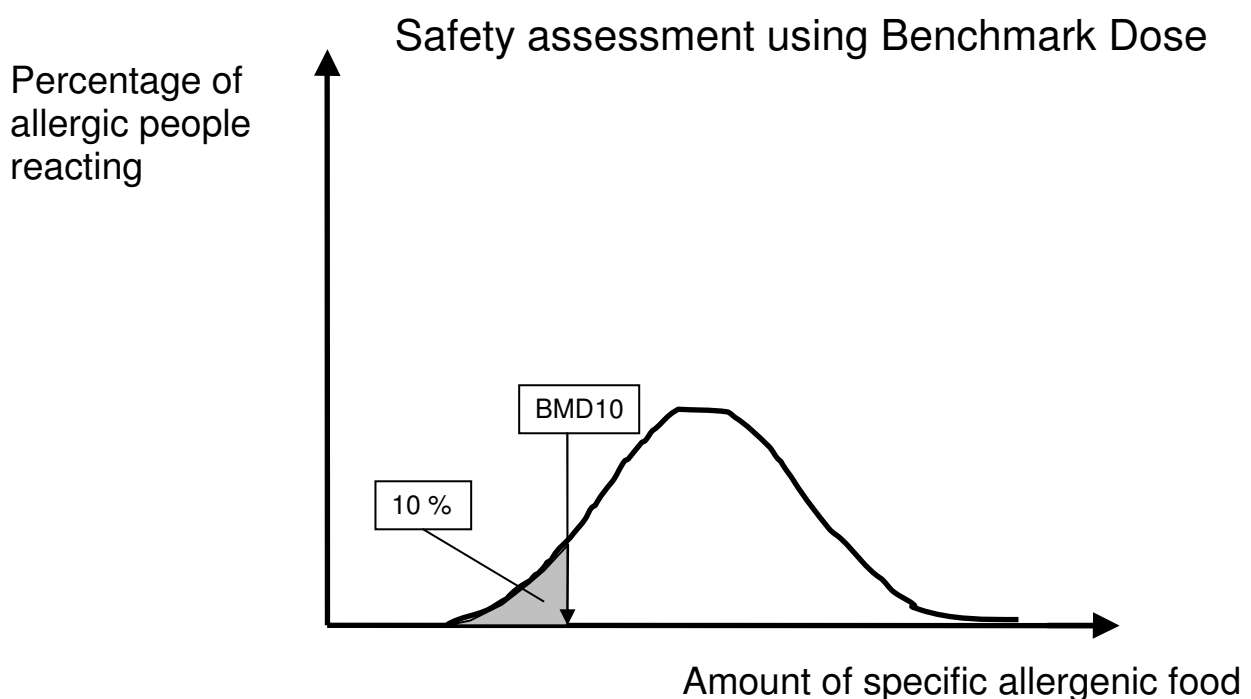
To decide on a safe level, scientists divide the NOAEL or LOAEL by 10 to 100. They do that to account for uncertainties in the DBPCFC data for example how well the limited data represent all food allergic people and how an allergic person might react on different occasions. The number they reach is an amount of allergenic food considered safe to eat for the majority of allergic people in general.

A strength of this approach is that it is easy to use. In addition it is not necessary to have data on what allergic people eat and in what amounts. A weakness of this approach is that it is dependent on how “correct” the NOAEL or LOAEL value is. A consequence of using the approach is that in practice it may be impossible for the food industry to attain and measure levels of allergenic food below the amount considered safe for allergic people.

The Australian Food and Grocery Council has developed and recommend the use of an allergen safety assessment tool based on this approach. The food industry can use this tool to be consistent when they warn allergic people of the unintentional presence of allergenic food using warning labelling. The Australian risk assessment tool, VITAL (Voluntary Incidental Trace Allergen Labelling), is available at: <http://www.allergenbureau.net/allergen-guide/vital/>

#### *Safety assessment using Benchmark Dose*

In this approach scientists use statistical models to create a graph of the available DBPCFC data of a certain allergenic food. From the graph they can calculate the amount of that allergenic food that will cause an allergic reaction in, for instance, 10 % of allergic people. Scientists call this amount of allergenic food for **BMD10** (Benchmark Dose for a 10 % incidence).



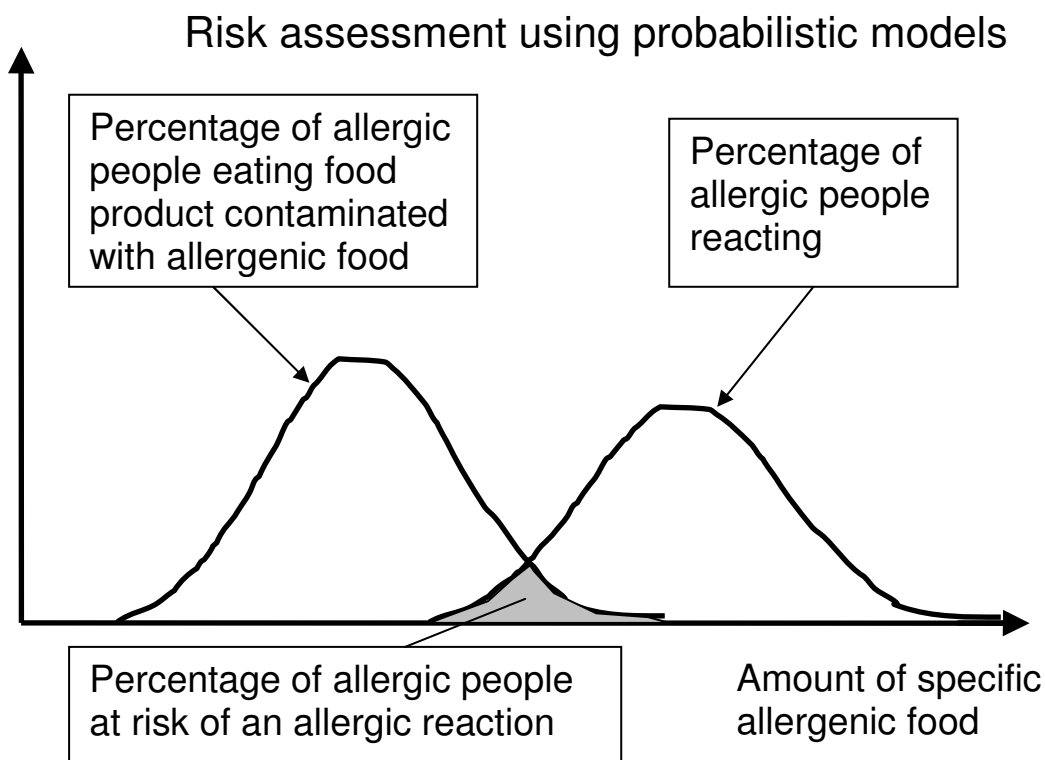
Scientists divide the BMD10 with an estimate of how much an allergic person may eat of an allergenic food to calculate the **MoE** (Margin of Exposure). Thus the MoE is a number that describe the safety or lack of safety of a given level of contamination with an allergenic food in a food product not meant to contain it. The larger the MoE, the safer the food product.

A strength of this approach is that it is relatively easy when scientists have established the BMD10 for a specific food to calculate the MoE for a specific contamination level in a specific food product. In addition a BMD10 value is in general more “correct” than a NOAEL or LOAEL value as scientists can use all the data available to arrive at the value. A weakness of this approach is that scientists need to be able to understand and use statistical models. Another weakness with the approach is that the MoE can only be calculated if data are available on what allergic people eat.

To my knowledge nobody has so far used this approach to assess the safety of a food product contaminated with an allergenic food.

### ***Risk assessment using probabilistic models***

In this approach scientists also use statistical models to create a graph of the available DBPCFC data. In addition they use statistical models to create a graph of the number of allergic people who eat various amounts of allergenic food. To do that, the scientists use knowledge or assumptions about how much allergic people consume of various foods and what the allergen contamination level is in those foods.



From the two graphs scientists calculate how many people are at risk for an allergic reaction.

A strength of this approach is that you can actually calculate a risk, that is the probability of allergic reactions in a population. In addition scientists use more data to arrive at the risk compared to the other approaches which in general should mean that the calculated risk is closer to the true risk. A weakness of this approach is that scientists need to be able to understand and use statistical models. Another weakness with the approach is that it needs data on what allergic people eat.

The Dutch scientists who developed this approach used it recently. They calculated how many milk allergic people in the Netherlands were at risk from allergic reactions to specific dark chocolate products contaminated with milk protein. Based on the result the company manufacturing the chocolate products changed their allergen management procedures.

### **The amount and quality of data**

For all of the approaches, scientists would like more and better data to be able to predict the safety of a food product with more certainty. The result of a safety or risk assessment is dependent on the amount and quality of data which scientists use. All three approaches use the same data from DBPCFCs. In approaches using the Benchmark Dose and probabilistic models, data on what allergic people eat is also necessary. The more accurate the data are, the more accurate will the result of the safety or risk assessment be. When the data are not as good as desired, scientists need to make use of assumptions. This of course means that the result of the safety or risk assessment will be less accurate and more uncertain.

### ***The quality of data from DBPCFCs***

So far very few DBPCFC studies have been conducted using the same method. In order to compare and combine individual data in a statistical model to predict safe dose limits for an allergic population, researchers need data from DBPCFC studies performed in a standardised manner. The challenge materials, the selection (and exclusion) of patients, and the challenge procedure are the major variables, which may affect the results. You can read much more about these issues in the article: “What amounts of foods may trigger food allergy symptoms?” by Pia Nørhede.

### ***The quality of data on what allergic people eat***

Many countries survey what people in the country eat. It is likely that food allergic people have different eating habits to other people in their country. They may try to avoid eating food products that they think may pose a risk to them. Therefore, collecting information about the dietary habits of people at risk of severe allergic reactions to foods might improve the quality of the eating data. However, no or very few scientists have surveyed specifically what allergic people eat.

As is the case for the DBPCFCs, scientists use many different methods to conduct food consumption surveys. In addition it is well known that the eating habits differ a lot between countries. So it is probably not a good idea to use data from one country to predict the risk of an allergic reaction in people in another country.

The above text is based on the paper:

C. B. Madsen, S. Hattersley, J. Buck, S. M. Gendel, G. F. Houben, J. O'B. Hourihane, A. Mackie, E. N. C. Mills, P. Nørhede, S. L. Taylor, R. W. R. Crevel (2009). Approaches to risk assessment in food allergy: Report from a workshop “developing a framework for assessing the risk from allergenic foods”. *Food Chem. Toxicol.* 47(2), 480-489.

*EuroPrevall is an EU-funded project about food allergy. The primary objective of EuroPrevall is to improve the quality of life for all food allergic consumers. To meet that objective EuroPrevall will conduct research to obtain information that we currently lack. EuroPrevall will also develop the tools necessary to manage food allergies more effectively. The 63 partners from 25 different countries include some of the leading allergy research organisations in Europe as well as clinical, patient, and industrial organisations. Visit [www.euoprevall.org](http://www.euoprevall.org) for more information on the project.*