Policy brief | April 2014

GM Food and allergies

African
Biosafety
Network of
Expertise

NEPAD Planning and Coordinating Agency








Brief background

Food allergies are generally associated with specific proteins in our diets. Thus, before a novel protein is allowed in our diets, careful consideration is given the possibility or otherwise that it may be allergenic. Some of the first generation GM plants (e.g. those with herbicide tolerance and insect resistance traits) were engineered to produce specific proteins which are responsible for their desirable traits. Thus, during the pre-market evaluation of these plants, the novel proteins are subjected to careful scrutiny on a case-by-case basis to eliminate any likelihood of causing allergies. In this brief, we explore the basics of food allergy in general and as it relate to these specific proteins in GM foods and we explore the underlying principles behind measures used by regulators to scrutinize proteins for allergenicity.

Food allergies

Food allergies are adverse reactions to an otherwise harmless food or food component and involve an abnormal response of the body's immune system to specific protein(s) in foods known as "allergens". Symptoms of food allergies may occur within minutes to a few hours after ingestion of the offending food and are varied in nature; they include rashes, wheezing, diarrhea, vomiting, stomach cramps, shortness of breath, itching of the mouth, throat, eyes, skin, or some combination of these responses. In rare cases, allergies may be life threatening and may result in rapid death unless emergency action is taken.

How food allergies arise

Humans have immune systems that defend our bodies against agents of diseases like viruses, bacteria or toxins. For some individuals, this natural defense mechanism is triggered by some components in food, i.e. specific proteins. This causes the person's immune system to mistakenly recognize a **normal food protein** as a threat to the person's health thus releasing antibodies called immunoglobulin-E (IgE) to fight off the "threat" (i.e. the protein). In the process, the body produces chemicals that trigger the symptoms of allergy described above. True food allergies are mostly mediated by IgEs and are different from **food intolerances** that are usually caused by a person's inability to digest or absorb certain foods e.g. intolerance to milk (lactose intolerance). Many reported cases of allergies are actually *food intolerances* which are more common. In fact, only a small percentage of the global population exhibits true food allergies (1 - 3% of adults and 4 - 6% of children).

Foods that commonly cause allergies

A typical food contains thousands of different proteins, most of which are safely consumed daily by everybody without problems. Out of these, only a very small number tend to elicit allergies in susceptible individuals and these are most commonly found in just a handful of food items including; *eggs, peanuts (ground nuts), tree nuts, shellfish, fish, soybean, milk, and wheat*. These are called 'the big eight' and are responsible for over 90% of the world's true food allergies. These allergenic proteins are typically **abundant in the food**, are relatively **stable to digestion** by pepsin and belong to a limited number of protein structural families.

Can GM food cause allergies?

There are **no known cases of food allergies** to any of the proteins in approved GM foods. That notwithstanding, *perceived* risks of allergies associated with GM food proteins should be considered on a case-by-case basis by regulators. Although the GM technique itself does not predispose foods to causing allergies, there are four possible scenarios that may present a potential risk of allergies in GM foods:

i) Transfer of proteins from known sources of human allergens;

The genetic modification technology involves transferring genes between organisms. In some cases, these genes produce proteins that are responsible for the desirable characteristics of the GMO e.g. Bt genes produces *Cry* proteins which confers insect resistance. If these transferred genes are sourced from organisms with a clear history of causing allergies in humans, there is some possibility that the resulting protein may also be allergenic. In other words, the possibility exists of an unintentional transfer of a known allergenic protein into the GM food. A good example is when scientists tried to improve the nutrient profile of soybeans using genes obtained from the Brazil nut (a known allergenic food). During the laboratory trials of the improved soybean, it was found (using current screening methods) that the protein transferred from Brazil nut was actually associated with allergies in susceptible individuals. In other words, the scientists unintentionally transferred a potent known allergen from Brazil nut into the soybean, in which case individuals who are allergic to this protein in Brazil nuts may have been accidentally exposed to same in the improved soybean. **The project was halted immediately at the laboratory stage and the improved soybean was never commercialized.** Thus, the transfer of genes from a source containing known human allergens is strongly discouraged unless proper testing is completed to ensure that the proteins produced by these genes are not allergenic.

ii) Transfer of proteins that closely resemble known allergens (cross-reactive proteins);

A similar risk to i) may occur if the transferred protein is nearly identical in amino acid sequence to a major allergenic protein. In such a case, IgE antibodies that are specific to this major allergen may then recognize and cross-react with (bind tightly to) the new near-identical novel protein and trigger the same type of allergic response. Proteins that share more than 50% identity to an allergen over the full-length are often cross-reactive and can elicit a significant reaction in allergic individuals.

iii) The transfer of some proteins from organism with no clear history of human consumption and unknown allergenic potential may present a moderate risk of sensitization and allergy;

Because the technology is very versatile, there is considerable flexibility in sourcing desirable genes. Thus, there will be instances where the genes transferred (and the protein produced) have limited or no prior history of use in foods. At this point, it is worth noting that any protein in food is considered capable of causing allergies, however, the risks are higher for new proteins that are abundant in the food, are stable to digestion by pepsin and are stable under conditions used to prepare the food.

The risk of a new protein becoming an allergen if it is not similar in sequence to any known food allergen (as described above), abundant or stable to digestion and/or processing is probably very low. However, there is no single definitive test to indicate whether a novel protein may be allergenic and for many new proteins the only way to know for certain if a new protein causes allergy is when someone develops a true allergy on exposure and so far, this has not been reported for any of the GM foods that have been commercialized (since 1996).

iv) Unintended increase in the levels of endogenous allergens during the genetic modification process;

Some food crops are known to contain native allergens, but a few like peanuts and soybeans more commonly cause food allergy. When commonly allergenic crops are improved through the GM technology, there is **in theory** the risk of an unintended change in the levels of the endogenous allergens. Although highly unlikely, there might be concerns that a significant increase in endogenous allergen levels may enhance the allergenic potential of the new crop. In

principle, any such increases in endogenous allergens beyond levels that are known to occur naturally (range of natural variation) are undesirable although this does not introduce a new risk, and the health implications are unclear. However, the usefulness of such information is still being debated internationally and there is as yet no consensus. In practice, it is easy to detect large changes in the levels of native allergens, but interpreting the results should be performed in the context of understanding the variation of allergen levels in the non-GM varieties of the same crop. Thus, in the unlikely case that a significant increase in endogenous allergens is demonstrated, regulators may request further testing or institute risk management measures as deemed necessary to protect the populace. These should however be on a case-by-case basis having weighed the risks and benefits and should be scientifically justifiable.

Are GM foods tested for their potential to cause allergies?

There are a series of laboratory and computational techniques available to help predict the likelihood that new proteins in foods may cause allergies. These techniques are based on our current knowledge of allergens; particularly their structure and behavior in biological systems. Thus new proteins are scrutinized in a stepwise, case-by-case manner for any sign that they may have any of the characteristics commonly associated with known major allergens. None of these tests done in isolation can provide conclusive evidence on the allergenicity potential of any new protein in GM foods. But collectively, they can help define a general probability (higher or lower likelihood) that a novel protein may cause allergies and thus collectively are described as a **'weight of evidence'** approach to allergenicity evaluation. Thus, regulators should weigh the evidence from the various tests to make an informed science-based decision on allergenicity. This 'weight of evidence' approach has proven effective so far and has been used for the past 17 years of GE food commercialization. In the next issue, we will discuss this approach to allergenicity testing in further details. It is important to recognize though that the major risks of food allergy are often easy to identify (transfer of an allergen or a likely cross-reactive protein) and also to recognize that it is theoretically possible that almost any dietary protein may be a food allergen for one person out of seven billion. The goal of risk assessment **cannot** be to exclude all risks, but rather it should be to minimize the major risks to a level that is acceptable.

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This brief was developed by the African Biosafety Network of Expertise (ABNE) to address food safety aspects of Modern biotechnology and is primarily for regulators, policy-developers and decision-makers.

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Working towards building functional biosafety systems in Africa

April 2014

ABNE April, 2013