



October 2012

Safety Assessment of Genetically Engineered Foods: US Policy & Current Science

Authors: Jennifer Kuzma & Rachel Haase, Humphrey School of Public Affairs; University of Minnesota.
Multidisciplinary review team and references available at z.umn.edu/PolicyBriefs

Summary of Findings:

- Safety of GE foods is evaluated through the U.S. Food and Drug Administration's voluntary consultation process.
- The FDA can take action if food, including GE food, presents a demonstrable safety risk post-market.
- GE safety studies focus on toxicity, adverse nutritional changes, allergenicity and horizontal gene transfer.
- Scientific studies testing whole GE food show some mixed results so statements about all GE foods being safe or unsafe are unwarranted.
- Whole-food feeding studies for GE safety assessment are tricky, as plant varieties are diverse in chemical composition and the effect of the introduced genes or changes caused by them are hard to tease out.
- Strong agreement exists for better testing protocols, especially for allergenicity and whole-food feeding trials.

Background

Genetically engineered (GE) or genetically modified (GM) foods continue to spark debate after nearly 20 years on the market. Genetic engineering allows for the transfer of genes from one organism to another, including transfers between different kingdoms (i.e. bacteria to plants). GE food crops have been grown in field trials in the U.S. since the mid-1980s and have been on the market since the mid-1990s. Most corn, soybeans, and cotton grown in the United States today are genetically engineered with herbicide tolerance or pest-resistant traits. The majority of processed foods on U.S. grocery shelves and animal feed products have been made from GE crops or their ingredients, except for certified organic foods which cannot be intentionally produced with GE crops or ingredients.

U.S. safety assessment policy

The Food and Drug Administration (FDA) has primary responsibility for the safety of food in the U.S. and can take action if a food presents a demonstrable safety risk post-market. GE food is regulated under the 1986 Coordinated Framework for the Regulation of Biotechnology (CFRB). The CFRB states that the product should be the focus of regulation and not process. The CFRB identified no new categories of risks associated with GE crops in comparison to non-GE crops; and found no new laws to be required for the regulation of GE crops, foods, and other products. FDA made a decision in 1992 to treat GE foods as "substantially equivalent" to conventional foods, unless there is reason to believe that they should be treated otherwise. Under this policy producers are voluntarily asked to submit data on GE foods to the agency through a consultation process. It is thought that the vast majority, perhaps all, of manufacturers of novel GE foods have gone through the FDA consultation process.

GE food safety assessment processes

U.S. federal agencies use health and environmental risk assessments for food safety regulatory decisions. Risk assessment uses available information on exposure and health consequences. Proponents of GE foods often argue that we have been consuming GE foods for two decades without observed adverse health consequences and that

there is no reason to single them out for more regulatory scrutiny than conventionally bred food. Opponents argue that we have not been looking hard enough for health consequences and that over long periods of time, low-level consumption may lead to chronic effects that go undetected in post market surveillance. Much of the disagreement comes down to whether people prefer “proof of safety” or “proof of harm” approaches to regulatory policy for GE foods.

What concerns are assessed with respect to the safety of GE foods?

1. Toxicity

- Toxicity is the potential that introduced genes could be toxic or the process of genetic engineering could disrupt native gene regulation and lead to increased production of natural toxins. FDA suggests screening for increases in existing or natural plant toxins. Screening can be done using genomic technology and biochemical assays (metabolomics). Toxicity studies have transitioned from feeding studies only testing the expressed protein to testing consumption of the whole food.

2. Adverse nutritional changes

- Adverse nutritional changes are changes in the nutritional composition of the food such as decreases in key nutrients or production of compounds that prevent nutrient uptake. Potential adverse nutritional changes in GE crops are analyzed in similar ways to toxicity. When the major nutrients, anti-nutrients, metabolites, and natural plant toxins found in GE foods are equivalent to the non-GE food, then safety assessment focuses on the specific protein(s) expressed from the introduced gene(s). For some types of GE-foods, such as vegetable oil coming from soybean or canola, the final food product is usually free of the engineered gene or its protein product.
- The evaluation of GE food products for toxicological or anti-nutritional properties using whole-food feeding studies has given some contradictory results. The American Medical Association reports on studies that showed toxic effects on liver and pancreas with certain herbicide tolerant (Ht) soybean varieties, but they also report that several studies show no effects with Ht or *Bacillus thuringiensis* (Bt – an insecticidal protein from a bacteria) engineered crops. In a systematic review of the scientific literature, Domingo et al. describe conflicting studies about whether a specific Bt corn variety is toxic to liver and kidneys. They note an almost equal number of studies showing no harm from GE foods or harm. In a recent longer-term study conducted over two years, Ht corn was found to have adverse hormonal and toxic effects when fed to rats at 11% of their diet.* However, previous longer term feeding studies have shown mixed results with GM crops: some have indicated no safety differences between GE and non-GE varieties, while others have demonstrated potential harm. Considerable controversy exists among scientists regarding whole-food feeding trials used to assess safety. Harmful effects from eating whole GE foods in safety trials might be due to natural variation in the biochemistry of the foods or un-natural diets being forced on test animals, rather than the introduced genes or changes caused by them, and these variables are hard to tease out of feeding trials with GE foods.

3. Allergic reactions

- Allergic reactions represent exaggerated human immune responses to normally harmless substances. Concerns about allergic reactions to GE foods peaked in 2001 when a Bt corn product approved for animal feed, Starlink, inadvertently entered the human food supply. The particular protein engineered into this Bt corn variety showed some similarity to known human allergens in its protein sequence. Some consumers reported adverse allergenic reactions but the link to Starlink corn was not confirmed. The controversy highlighted the limits of regulatory compliance for mixing unapproved and approved varieties, as well as the difficulties of predicting allergenicity of novel GE foods. Experts in this area have called for the development of animal testing models to predict the allergenicity of foods.

*The scientific paper documenting these findings was retracted under controversy by the journal Elsevier without evidence of fraud or misconduct.

4. Horizontal gene transfer

- Horizontal gene transfer involves the transfer of genetic materials from one organism to another other than its offspring. People eat genes (made of DNA) all the time in food and the question is whether these genes can transfer from the GE food to humans or human gut bacteria and, if so, what are the consequences? Of particular concern are antibiotic resistance genes whose transfer might make gut bacteria resistant to certain antibiotics. Although GE crop producers are starting to phase out these genes, they are still widespread in GE crops on the market. To date, there is no evidence for the uptake of digested DNA by gut bacteria after consumption of food, although few studies have addressed this possibility. Recent studies suggest that genes from GE foods can survive in the gut environment and enter the bloodstream, so uptake by gut microbes is a possibility. The rate and consequences of uptake remain unknown.

Summary

Disagreement exists on the best process of assessing GE food safety and whether more or less precautionary approaches should be taken to regulatory testing and policy. The meaning of safety itself is contentious. Research methods for assessing safety and detecting risk are actively debated. There is broad agreement that improved testing protocols are needed; testing should be done on a product by product basis; and that blanket statements about all GE foods being “safe” or “unsafe” cannot be made based on the current science.

References

1. Office of Science and Technology Policy (1986). Coordinated Framework for the Regulation of Biotechnology. Federal Register 51 (123): 23302-23350.
2. FDA (1992). Statement of Policy: Foods Derived from New Plant Varieties,” Federal Register 57 (104): 22984-23005.
3. AMA (2012). Action of the AMA House of Delegates 2012 Annual Meeting: Council on Science and Public Health Report 2.
4. Domingo, J.L., & Bordonaba, J.G. (2011). A literature review on the safety assessment of genetically modified plants. *Environment International* 37(4), 734-742.
5. Seralini, G. et al. (2012). Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize. *Food and Chemical Toxicology*.¹
6. Snell, C. et al. (2011). Assessment of the health impact of GM plant diets in long-term and multigenerational animal feeding trials: a literature review. *Food and Chemical Toxicology*. 50, 1134–1148.
7. Centers for Disease Control and Prevention. (2001) Investigation of Human Health Effects Associated with Potential Exposure to Genetically Modified Corn: A report to the FDA
8. Sutton SA, Assa'ad AH, Steinmetz C, Rothenberg ME. (2003) A negative, double-blind, placebo-controlled challenge to genetically modified corn. *Journal of Allergy and Clinical Immunology*, 112, 1011-2.
9. Taylor SL. (2006) Review of the development of methodology for evaluating the human allergenic potential of novel proteins. *Mol Nutr Food Res* 50:604-9; Codex Alimentarius Commission. (2003) Alinorm 03/34: Joint FAO/WHO Food Standard Programme, Codex Alimentarius Commission, Twenty-Fifth Session, Rome, 30 June–5 July, 2003. Appendix III, Guideline for the conduct of food safety assessment of foods derived from recombinant-DNA plants and Appendix IV, Annex on the assessment of possible allergenicity.
10. Rizzi A, Raddadi N, Sorlini C, Nordgrd L, Nielsen KM, Daffonchio D. (2012) The stability and degradation of dietary DNA in the gastrointestinal tract of mammals: implications for horizontal gene transfer and the biosafety of GMOs. *Critical Reviews in Food Science and Nutrition* 52:142-61.

*The scientific paper documenting these findings was retracted under controversy by the journal Elsevier without evidence of fraud or misconduct.