THE NATIONAL ACADEMIES
REPORT IN BRIEF

Safety of Genetically Engineered Foods

Approaches to Assessing Unintended Health Effects

Genetic engineering is one of the newer technologies available to produce desired traits in plants and animals used for food, but it poses no health risks that cannot also arise from conven-tional breeding and other methods used to create new foods. Any method could result in unintended changes in the composition of the food. The report concludes that all altered foods should be assessed on a case-by-case basis before they are sold to the public to determine whether unintended changes in the composition of the food could adversely affect human health.

Genetic engineering is a subset of the broad array of techniques available to produce desired traits in animals, plants, and microorganisms used for food. First patented in 1980, genetic engineering is the process of manipulating a gene using recombinant DNA (rDNA) methods.* Today, foods with ingredients developed with the aid of genetic engineering (GE foods), such as some cereals, snack foods, and soft drinks containing modified corn and soy ingredients, have become more common.

The process of genetic engineering has not been shown to be inherently dangerous, but rather, evidence to date shows that any technique used to create new foods carries the potential to result in unintended changes in the composition of the food.

Safety of Genetically Engineered Foods: Approaches to Assessing Unintended Health Effects assists policymakers in evaluating appropriate scientific methods for detecting unintended changes in food and assessing the potential for adverse health effects from GE products before they are sold to the public.

Examples of Unintended Changes

Foods, whether or not they are genetically engineered, carry potentially hazardous substances that must be assessed for safety. Breeding and other alteration methods can sometimes increase the levels of these hazardous substances. For example, celery

Methods for Introducing New Traits into Plants

Genetic engineering is a subset of the many methods used to introduce new traits into plants and animals. Some of those methods are listed below.

Non-GE Methods (Non-targeted)

Simple Selection: Plants with desired traits are selected for continued propagation.

Crossing: Brushing pollen from one plant onto a sexually compatible plant to produce a hybrid with genes from both parents.

Embryo Rescue: Placing a plant that has naturally cross-pollinated into a tissue culture environment to enable its full development.

Mutagen Breeding: Exposing plants or seeds to mutagenic agents (e.g., ionizing radiation) or chemicals to induce random change in the DNA sequence; new plants are assessed for valuable traits.

GE Methods: (Targeted)

Microbial vectors: Takes advantage of a microbe's ability to transfer and stably integrate segments of DNA into a plant so that the plant then expresses those traits.

Electroporation: Plant cells growing in culture are stripped of their protective walls; DNA is then supplied to the medium and electric shock used to destabilize the cell membrane and allow DNA to enter.

*Recombinant DNA methods enable the insertion of a gene or gene sequence in an exact place in the DNA of the new host, thus producing a targeted result.

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naturally produces psoralens—irritant chemicals that deter insects from feeding on the plant. Celery plants with elevated levels of psoralens suffer less damage from disease and insects and appeal more to consumers, and therefore, had been selectively bred. Unfortunately, workers who harvested high psoralen-producing celery or packed it in grocery stores had, on occasion, developed severe skin rashes, especially if they were exposed to bright sunlight.

Foods that are new to humans, whether conventionally bred or genetically engineered, can also create potential health issues. Kiwi fruits, originally an edible but unpalatable plant from China, were conventionally bred in New Zealand to become the fruit we know today that was introduced to the United States in the 1960s. Some people who were not previously exposed to kiwi developed an allergic reaction to it.

Many mechanisms of conventional breeding are common to both genetic engineering and other genetic modification techniques. For organisms genetically engineered using rDNA techniques, some possible mechanisms of unintended change include the following:

- The sequence of interrupted DNA may be a functional gene, resulting in a loss or gain of whatever function the gene provided.
- Chromosomal changes may occur depending on where the genes were inserted.
- Spontaneous mutation may occur.

The committee evaluated the likelihood for an unintended health effect to occur as a result of various methods of genetic modification. Genetic engineering was placed on a continuum with other forms of genetic alteration (see Figure 1). The committee's analysis of

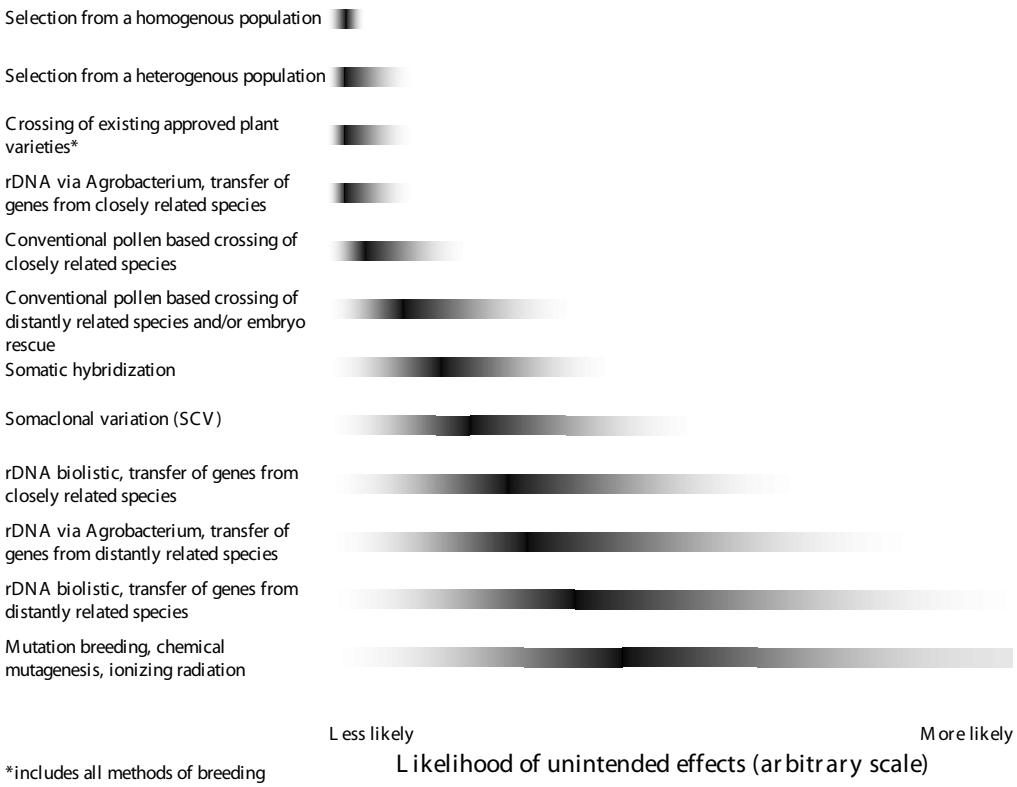

Figure 1. This continuum shows the relative likelihood of unintended genetic effects—any unintended effects, not necessarily those associated with health effects—associated with various methods of plant genetic modification. The gray tails show the range of potential unintended changes; the black bars indicate the relative degree of genetic disruption for each method. Of the methods shown, selection from a heterogenous population is the least likely to express unintended effects, and the range of those that do appear is quite limited. In contrast, induced mutagenesis is the most genetically disruptive, and produces a wide range of effects.

this process determined that the method used should be considered, but it should not be the sole criterion for evaluating possible health effects associated with unintended changes.

Methods for Detecting Unintended Changes

The harm to health from any compositional changes in foods depends on the nature and biological consequences of the compounds produced, not the method by which the changes were made. The traditional approach of determining the presence and quantity of compounds is targeted quantitative analysis, where scientists test for the presence or amount of compounds or class of compounds. During the past decade, traditional analysis has become much more sophisticated in separating and quantifying nucleic acids, proteins, and other small molecules, although more improvements are still needed.

New methods of identifying genes, including genomics, proteomics, and other profiling techniques, are now being applied and hold much promise for detecting unintended changes. These "high throughput" methods provide an enormous amount of data for a given organism, tissue, or food product. However, there is still a significant learning curve to scale in order to interpret the biological relevance of this data. Until more is known, the use of these techniques is limited for predicting and assessing unintended adverse health effects of GE foods.

Current Safety Assessments

The current safety assessments used before putting GE foods on the market focus on comparing a GE product with its conventional counterpart to identify uniquely different components. Comparisons are made using traditional analytic techniques and also with agronomics, which is the comparison of physical characteristics of the plant. Any significant difference is noted, even those with a perceived benefit, for example, an increased level of a nutrient or other naturally-occurring compound in the food product. Animal feeding trials are also sometimes used to detect any health effects in animals that might be signals for adverse effects in humans.

The most appropriate time for a safety assessment of new food is in the premarket period, although safety assessments may continue after market release, generally for products that are not equivalent to their conventional counterparts or that contain significantly altered nutritional and compositional profiles. Although post-market surveillance has not been used to evaluate any of the GE products currently on the market, it is a promising approach to use in monitoring potential anticipated or unanticipated effects.

The report proposes a new framework that could be used to examine, identify, and evaluate systematically the unintended compositional changes and health effects of all altered foods, including GE foods (see Figure 2). This framework is based on methods to identify appropriate comparators; increase the knowledge of the determinants of compositional variability; increase understanding of the biological effects of secondary metabolites in foods; develop more sensitive tools for assessing potential unintended effects from complex mixtures; and improve methods for tracing exposure to such altered foods.

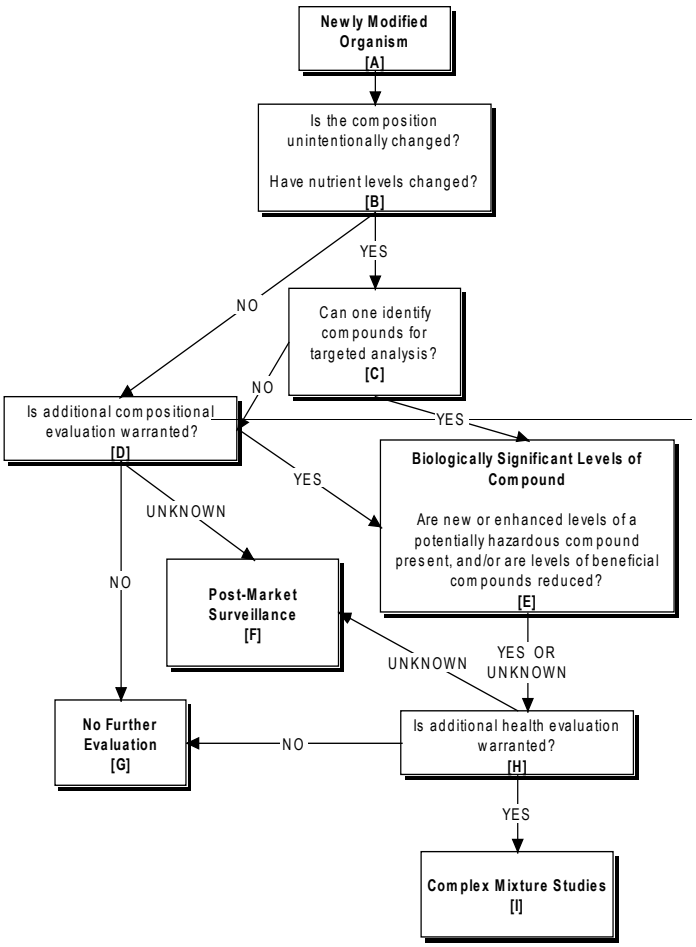

Figure 2. A flowchart for determining potential unintended effects from genetically altered foods.

Maintaining a Safe Food Supply

The report recommends that unintended compositional changes resulting from alteration, particularly genetic engineering, should be assessed on a case-by-case basis. Modified foods should be assessed only when warranted, based on the presence of novel compounds or altered levels of naturally occurring compounds above those found in the unmodified counterpart, taking into account the organism modified and the nature of the introduced trait. The report specifically recommends that:

- Appropriate federal agencies determine whether evaluation for potential health effects of genetically altered foods, including those that are genetically engineered, is warranted by elevated concern, such as identification of a novel substance in the food or levels of a naturally occurring substance that exceeds the range of recommended or tolerable intake.
- Standardized sampling methodologies, validation procedures, and performance-based techniques for targeted analyses and profiling of all altered food, including genetically engineered, should be developed and used.
- For those foods warranting further evaluation, a safety assessment should be conducted prior to commercialization.
- Post-commercialization validation of premarket testing should occur where safety concerns are present.
- Improved tracing and tracking methods should be implemented for genetically engineered foods, when warranted by changes such as significant compositional differences with non-GE counterparts, in specific populations of consumers, or unexplained clusters of adverse health effects.

Need for Additional Research

A significant research effort should be made to support analytical methods technology, bioinformatics, and epidemiology and dietary survey tools to detect health changes in the population that could result from genetic alteration and, specifically, genetic engineering of food.

Research is also needed to determine the relevance to human health of dietary constituents that arise from or are altered by genetic modification. This includes developing new tools that can be used to assess potential unintended adverse effects, improved DNA-based immunological and biochemical tags for selected altered foods entering the marketplace, and improved techniques that enable toxicological evaluation of whole foods and complex mixtures.

Committee on Identifying and Assessing Unintended Effects of Genetically Engineered Foods on Human Health: Bettie Sue Masters (Chair), University of Texas Health Science Center; **Fuller W. Bazer**, Texas A&M University; **Shirley A.A. Beresford**, University of Washington; **Dean DellaPenna**, Michigan State University; **Terry D. Etherton**, The Pennsylvania State University; **Cutberto Garza**, Cornell University; **Lynn R. Goldman**, Johns Hopkins Bloomberg School of Public Health; **Jesse F. Gregory**, University of Florida; **Jennifer Hillard**, Consumer's Association of Canada, **Alan G. McHughen**, University of California, Riverside; **Sanford A. Miller**, Virginia Polytechnic University; **Stephen L. Taylor**, University of Nebraska; **Timothy Zacharewski**, Michigan State University; **Ann Yaktine** (Study Director), Institute of Medicine.

This report brief was prepared by the National Research Council's Board on Agriculture and Natural Resources and Board on Life Studies of the Division on Earth and Life Studies and the Institute of Medicine's Food and Nutrition Board based on the committee's report. For more information, contact the Board on Agriculture and Natural Resources at (202) 334-3062. *Safety of Genetically Engineered Foods: Approaches to Assessing Unintended Health Effects* is available from the National Academies Press, 500 Fifth Street, NW, Washington, DC 20001; 800-624-6242; www.nap.edu.