LEAGUE OF WOMEN VOTERS®

Genetic Engineering and Genetically Modified Organisms in the Food System

Genetic Engineering: Definitions

The discovery of DNA and research in genetics and molecular biology in the mid-twentieth century made possible a new approach to both plant and animal breeding through genetic engineering: the alteration of genetic material through direct manipulation of the DNA sequence. While the term "genetic engineering" (GE) is sometimes used to include anything from controlled hybridization to chemically or radioactively induced mutations, the following USDA definition suggests the most common usage of the term:

> *Genetic engineering is the manipulation of an organism's genes by introducing, eliminating or rearranging specific genes using the methods of modern molecular biology, particularly those techniques referred to as recombinant DNA techniques.*[1]

Two related terms include:

Transgenesis/Recombinant DNA Technology: involves recombining the insertion of one or more individual genes between organisms/species to create a new organism. The resultant organism is "transgenic," otherwise known as a genetically modified organism (GMO).

Cisgenesis: This form of genetic engineering transfers genes between closely related organisms that could otherwise be conventionally bred, using the same techniques that are used to produce transgenic organisms. This technique speeds the breeding process, allowing specific modifications to be accomplished much more quickly.

Genetic engineering is utilized to induce characteristics that could: generate a higher yield for the crop; provide disease, insect or herbicide resistance; enhance nutritional value; allow plants to thrive under unfavorable growing conditions such as cold, drought or soil salinity; increase pharmaceutical value; or create a plant more effective for phytoremediation (pulling pollutants from soil or water). While many of these objectives can be accomplished through traditional hybridization techniques, new varieties can often be created more quickly and in a more targeted way through genetic engineering.[2]

An understanding of the basic principles is important because confusion arises when people generalize and use terms like biotechnology, genetic engineering (GE) and genetic modification (GM) interchangeably. For clarity, this segment will use, "GE" or "GM" (without a following noun) to refer to any of several technical *processes or techniques* for transferring genes between

species (transgenesis). Whereas, the use of "GMO" or "GE" or "GM," with a corresponding noun, will refer to any organism, food, crop, animal, etc., resulting from such a genetic transfer.

Evolution of GE applications in the United States

The earliest advances in GE were in the pharmaceutical field. Insulin derived from recombinant DNA was first marketed in 1978, followed by the first genetically engineered vaccine in 1984. The first GE food application was genetically modified rennet, approved for use in cheese in 1990.[3] In 1994 Calgene received FDA approval to market the first GE food crop—the *Flavr Savr* tomato—which had been submitted for FDA review in 1992. This was followed by the introduction of several GE crops in 1995: insect resistant (Bt) corn; herbicide resistant (Ht) soybeans, virus resistant squash, canola with modified oil composition, and an Ht cotton.[4] The same year also marked the regulatory approval of the first "stacked" GE seed, which was a cotton seed containing both a Bt and an Ht gene. Stacked seeds are also known as multiple stacked trait seeds (MSTs); they employ multiple genetically engineered genes and may combine one or more Ht and Bt combinations. Stacked seeds can provide resistance to multiple insects (a proposed response to the emerging problem of Bt resistance) while at the same time providing tolerance to various formulations of herbicide (currently, glyphosate or glufosinate).[5] As of 2013, stacked crops accounted for more than half of all U.S. corn or cotton.[6] Genetic engineering is also being used to develop potatoes and apples that resist browning, such as the non-bruising potato submitted for FDA and USDA approval in May 2013 (this is an example of *cisgenesis*, where genes from the same species are used).[7]

To date, FDA reports having completed 98 reviews of GE crops or traits proposed for commercialization.[8,9,10] Farmers have rapidly adopted GE crops and expanded their production; by 2013, GE cotton and corn represented 90% of planted acreages while soybeans and canola represented 93 percent of respective acreages.[11] According to the Grocery Manufacturing Association, "70% to 80% of the food we eat in the United States, at home and away from home, contains ingredients that have been [produced from] genetically modified [crops]."[12] GMOs are also expanding worldwide; a record 170.3 million hectares of biotech crops were grown globally in 2012, up 10.3 million from 160 million hectares in 2011, with adoption growing faster in developing (11%) than in industrialized (3%) countries.[13]

Ht and Bt Crops

The most widely used GE crops incorporate gene coding for a glyphosate resistant enzyme from the bacteria *Agrobacterium tumefaciens*. This practice creates herbicide tolerant crops (or Ht crops) that can be sprayed with glyphosate without harm to the crop; glyphosate is commonly found in weed killing products such as Roundup. Farmers have adopted Ht crops because they offered less spraying, less traffic on the field, and lower operating costs.[14] Ht crops allow farmers to practice no-till methods, thereby reducing soil erosion and runoff. Over time, monoculture methods, that use only these GE seeds and do not rotate crops, can create a field situation that is selective for the development of "superweeds" which are resistant to the herbicide.[15] As a result, herbicide use, including more toxic herbicides, may increase. Because the databases on pesticide

use are weak and researchers differ over the choice of analytical methods, there are contrasting results on pesticide trends and impacts in the literature for the US[16,17] and globally[18] even when the same time period is covered.

Another common GE trait makes use of genetic material from a naturally occurring bacterium, *Bacillus thuringiensis* (Bt), which is often used by organic farmers because of its natural origin and low toxicity to humans and animals. The resultant Bt crops are resistant to insect predation, which means increased yields and less money spent on post-planting applications of insecticide for many farmers.[19] The rapid growth in reliance on Bt for insect control, following the introduction of GE crops, appears to be contributing to rootworm resistance to the Bt rootworm trait, while a second major corn pest targeted by a Bt trait—the corn borer—has not shown resistance.[20,21,22] Although the threat of resistance can be reduced by good management practices, such as planting non-GE refuge crops, there is debate about the size of refuge areas needed and concern that recommended refuge practices are not always used or effective.[23]

Potential Ancillary Concerns: Research on environmental impacts of Bt crops has focused on the possibility that beneficial insects or animals (e.g., bees and bats) will be harmed by ingesting the crops or pollen; while some studies have documented problems, others have found that the effect on non-target insects is minimal.[24, 25] Studies have also been conducted on the animal health impacts of consuming Ht and Bt products. While many studies have found no negative health impacts,[26] there are some peer-reviewed studies that have identified problems in animals, leading their authors to call for more health impacts research and improvements in research methods.[27, 28]

The spread of Ht and Bt crops has raised concern about exposure to GE pollen contamination of non-GE crops. Alfalfa pollen can be carried as far as five miles by wind drift or movement of bees; GE sugar beet pollen can cross pollinate not only non-GE sugar beets, but also Swiss chard and table beets. There are two potential problems for farmers: (1) the possibility that unintended genetic modification may result in loss of income because farmers cannot sell contaminated products in their target market at the higher prices usually offered for non-GE products and (2) the possibility that a manufacturer would sue a farmer whose crop was unintentionally contaminated. The latter issue has been partially resolved with Monsanto pledging not to prosecute unintended contaminations.[29] The question of compensation is being dealt with by a few pending lawsuits seeking manufacturer compensation for past or potential income losses,[30] by specialists in agricultural law who are evaluating the various legal options for facilitating the co-existence of GE and non-GE farms,[31] and by a USDA Advisory Committee on Biotechnology and 21st Century Agriculture which issued its report in November of 2012.[32]

Disease Resistant Crops

While Ht and Bt crops focus on increased yield through minimized damage from insects or weed competition, other GE crops focus on other potential advantages. Disease resistance is a major area of investigation. GE papaya was developed in Hawaii in response to the papaya ring spot virus, which threatened the Hawaiian papaya supply.[33] Six varieties of GE yellow squash and zucchini currently on the market were engineered to resist three different viruses.[34] Work is

underway to develop GE oranges before the Florida orange succumbs to the green wilt virus,[35] and to create a GE banana resistant to the devastating viruses that threaten the global banana supply.[36] There have been efforts to develop virus resistant sweet potatoes and cassava in Africa, but the longevity of the resistance was found to be shorter than anticipated and yields lower than conventional varieties during the field testing phase; no commercial distribution has taken place to date.[37]

Biofortification

Biofortification involves breeding food to enhance the nutritional quality for the staple crops that many of the world's poorest people rely on for most of their calories. Examples of biofortification include increasing the protein, vitamin A, mineral, or folic acid content of foods.[38] In many cases, conventional breeding is being used successfully to enhance the nutritional quality of staple foods (e.g., vitamin A in sweet potatoes or zinc in wheat and rice).[39] However, there are biofortification goals that cannot be accomplished through conventional breeding such as increasing the vitamin A content of rice, which is the most common staple cereal worldwide. This gap led to the development of Golden Rice and research on biofortification through genetic engineering for other crops and traits not easily addressed using conventional breeding.[40, 41]

Regulatory Framework for GE Crops

The early expansion of the use of GE in plant production and the use of GMOs in processed foods was supported by federal policies. The Supreme Court affirmed the practice of patenting a GE living organism (*Diamond v. Chakrabaty*, 1980) when it decided that the human-made, genetically engineered bacterium, created by Chakrabaty, could be patented. The bacterium had the potential to break down multiple components of crude oil and, therefore, held great promise for cleaning up oil spills. The ability of individuals and firms to patent gene traits and GMOs provided incentives for investment in GE research and development.[42,43]

In 1984, the Reagan Administration proposed a "Coordinated Framework for the Regulation of Biotechnology" based on three central tenets:

1. U.S. policy would focus on the product of GM techniques, not the process itself;
2. Only regulation grounded in verifiable scientific risks would be tolerated;
3. GM products are on a continuum with existing products and, therefore, existing statutes are sufficient to review the products.[44]

The Coordinating Framework and subsequent implementation placed the responsibility for safety and regulation of food and feeds modified via genetic engineering under the FDA, which formally issued its policy for ensuring the safety of foods derived from genetic engineering in 1992.[45] Under this policy, the USDA Animal and Plant Health Inspection Service (APHIS) regulates the importation, interstate movement, and environmental release of transgenic plants

with the goal of protecting existing crops from hazards and assuring that GM plants and animals are safe to produce. The EPA registers pesticide products in transgenic plants prior to their distribution and sale and establishes pesticide tolerances for residues in foods.[46,47]

Substantial Equivalence

Regulation of GMOs is based upon the concept of *substantial equivalence*, wherein products are evaluated by regulatory agencies in a manner that compares them to conventional (non-GM) products or processes.

> *If a new food is determined to be substantially equivalent in composition and nutritional characteristics to an existing food, it can be regarded as being as safe as the conventional food (FDA, 1992; Kuiper et al., 2001; Maryanski, 1995; OECD, 1993) and does not require extensive safety testing. The evaluation of substantial equivalence includes consideration of the characteristics of the transgene and its likely effects within the host, as well as measurements of protein, fat and starch content, amino acid composition, vitamin and mineral equivalency, along with levels of known allergens and other potentially toxic components*.[48,49,50,51]

Although the concept of substantial equivalence is a starting point for the safety assessment for GM foods that is widely used by national and international agencies - including the Canadian Food Inspection Agency, Japan's Ministry of Health and Welfare and the U.S. Food and Drug Administration, the United Nation's Food and Agriculture Organization, the World Health Organization and the OECD,[52] some scientists and organizations object to the concept. A much quoted discussion, published in *Nature* in 1999 asserts:

> *The concept of substantial equivalence has never been properly defined; the degree of difference between a natural food and its GM alternative before its 'substance' ceases to be acceptably 'equivalent' is not defined anywhere, nor has an exact definition been agreed by legislators. It is exactly this vagueness that makes the concept useful to industry but unacceptable to the consumer.*[53]

Approval Process

The approval processes used by various agencies (FDA, USDA, EPA) varies,[54] yet they all aim at providing risk assessment to eliminate or minimize potential harmful consequences. The following material is from the USDA/APHIS process for getting a new GE plant to market, drawing on an APHIS Question & Answer Brief[55] and the results of a National Research Council (NRC) 2002 study of APHIS risk assessment.[56] Before a transgenic crop can be grown outside a laboratory, it must receive APHIS approval. The study evaluated the existing notification, permitting, and deregulation procedures and recommended the addition of post-deregulation monitoring. Their findings are summarized below.

***Notification and Permitting*:** Notification and permitting are two ways to obtain APHIS approval for field testing new products. Currently almost all field testing is conducted through the notification process. Within 30 days of notification of intent to move to field testing, an

APHIS staff member must determine if the information provided by the firm is sufficient to justify field testing the product; and the process involves no public or external scientific input. The NRC review found that "…the notification process is conceptually appropriate, but there is a need to reexamine which transgenic plants should be tested and commercialized through the notification process…" versus which should be required to go through the more intensive permitting process. If APHIS determines that there is a need to pursue a permit and conduct a formal Environmental Assessment of the plant, a description of the application is published in the Federal Register and is open to public comment. The permitting process was not commonly used at the time of this Agriculture Update.[57]

Deregulation: This is the final step to having a crop officially approved for commercialization by APHIS. Because GM seed is not made available by manufacturers for independent research until after a product has received market approval, regulatory decisions are based largely on data and analyses provided by the manufacturer. The 2002 review committee found:

> *"…that the APHIS process should be made significantly more transparent and rigorous by enhanced scientific peer review, solicitation of public input, and development of determination documents with more explicit presentation of data, methods, analyses, and interpretations."[58] [The report noted that] "… the extent of confidential business information (CBI) in registrant documents sent to APHIS hampers external review and transparency of the decision-making process."[59]*

The committee reported, however, that it was "not clear that APHIS has the power to decrease the unwarranted use of CBI" but noted that "regulatory agencies of other countries receive documents with less CBI than does APHIS."[60] Industry views CBI as a necessary tool to protect commercial interests in the rapidly developing field of gene technology.

Licensing agreements after product commercialization also place some restrictions on researchers that are not imposed for research for non-GE seeds. Following a 2009 complaint by 26 public sector research scientists regarding lack of access, major seed companies drafted new principles governing research and seed use, offering more open use of seed for research purposes.[61]

Post-deregulation monitoring. As currently implemented, APHIS deregulation is absolute; the agency does not assume further oversight of the plant or its progeny and descendants.[62] The NRC committee, however, found several compelling arguments for validation-testing and ecological monitoring after commercialization, recommending post-deregulation monitoring by APHIS to address issues such as scaling up the technologies and assessing unanticipated or long-term, incremental environmental impacts of transgenic crops.[63]

Public Views on the GMO Regulatory Processes and Findings

Public views on the health and environmental safety of GE products marketed in the US and the adequacy of the regulatory framework come from peer reviewed journal articles and the popular press. Critics of the review process maintain that participation is voluntary, testing is done by the

applicants, as opposed to the agencies themselves, and responsibility for safety rests, in most cases, with the individual developers. Developers believe that the process is really mandatory (though labeled "voluntary"), rigorous, highly prescribed, and data generation is both time consuming and costly, with an average price per approval of $136 million over 13.1 years.[64] The reasons for the differing points of view are well explained in a recent Grist.org blog, which concludes, surprisingly, that both sides are correct.[65]

A recent review of the GE literature by Nicolia et al. concluded that the majority of peer reviewed papers do not indicate a health risk for animals or humans consuming GE products nor provide evidence of environmental hazards.[66] Also, official statements by regulatory agencies in many countries and organizations with acknowledged scientific credentials (e.g., The US National Academies, the American Medical Association, the World Health Organization, the Royal Society, the European Commission, and Center for Science in the Public Interest) all agree that there is no evidence that it is dangerous to eat genetically modified foods. Recently, science-oriented publications including *Nature* and *Scientific American* also concluded there is no evidence that GMOs are bad for us. The statements concerning the absence of evidence that GE foods pose health risks, however, are generally accompanied by calls for continued vigilance because it is impossible to prove anything absolutely safe.[67]

Despite the above assurances of safety and statements such as "Several *trillion* meals containing genetically engineered food ingredients have been consumed by people around the world, with not a single adverse effect documented,"[68] concerns continue to be raised about GE risk assessment. In response to discussions in the popular press about a growing consensus among scientists on GE safety, 97 scientists have published a statement to say that such a consensus does not exist.[69] Epidemiologists point out, for example that it is difficult to actually study the link between GMOs and adverse effects in the US due to the absence of GMO product labeling as this means that "…people don't know whether they've actually consumed [GMOs]."[70] Others point to weaknesses in individual studies,[71,72,73] while some have described perceived flaws in assessment protocols,[74,75] and yet others have critiqued those having critiqued.[76] Others mention knowledge gaps in scientists' understanding of gene sequencing and interrelationships and their understanding of how genetic expression is turned on and off; this has led to research on methods for assessing the risk from complex exposures that might include GE foods, animal antibiotics and hormones, pesticide residues, nanomaterials, and novel food processing materials in addition to a myriad of other factors.[77,78]

GE Animals

The first GE application in animals took place in 1974, when viral DNA was inserted into a mouse embryo to create a transgenic mouse. GE mice have since been used for research on human disease and pharmaceutical testing. While more than forty different breeds of animals have been genetically engineered, for research and medical purposes, as of yet, none have been approved for market release as human food.[79] Traits being developed include "improved milk

production and composition, increased growth rate, improved feed utilization, improved carcass composition, increased disease resistance, and enhanced reproductive performance."[80]

FDA Guidelines

In 2008, the FDA provided guidelines for the regulation of transgenic animals, premising the rules on the agency's authority to regulate new drugs. The FDA considers the recombinant DNA (rDNA) construct to be a new animal drug because it is an article intended to alter the structure or function of the animal. New animal drugs may be approved if they are shown to be safe and effective for the intended use. The agency examines the safety of the rDNA construct to the animal, the safety of food from the animal, and any environmental impacts posed (safety issues), as well as the extent to which the performance claims made for the animal are met (efficacy issues).[81,82] When these guidelines were made public, they were met with expressions of concern about transparency, the labeling of GE animal products, and the lack of agency oversight capacity with regard to environmental impact.[83]

Animal clones produced through the use of genetic engineering are regulated under the same new animal drug provisions as any other transgenic animal. "Clones produced using a species' own DNA are considered equivalent to conventionally bred animals; cloned cattle, pigs, and goats may be sold as part of the food supply without labeling."[84,85]

Commercial Food Applications

Commercial food applications predicted in the early years of GE work in animals have so far been elusive. "For example, many of the early transgenic livestock studies produced animals with a range of unexpected side effects including lameness, susceptibility to stress, and reduced fertility."[86]

Regulatory hurdles and consumer acceptance of GE animals in the food chain has also discouraged research and development investment (e.g., the case of the Enviropig™),[87,88] but rapidly declining stocks of fish worldwide[89] have spurred significant research on GE fish such as AquaBounty's salmon, which grows twice as fast as wild salmon as a result of inserting genes from other fish.[90],[91] AquaBounty's salmon have been slowly nearing FDA approval[92] after more than two decades of research and an investment of over $60 million. Consumer groups, including Consumers Union and Food & Water Watch however, have petitioned the FDA to assess the GE fish as a food additive, rather than an animal drug, and have expressed concerns about the transparency of the review process and the adequacy of the analysis of health impacts.[93,94] The FDA responded to some of these concerns by arranging an open meeting and providing more data and information about the decision process.[95] There has also been some discussion of potential environmental impacts if the GE fish escape and mate with wild fish. Scientific studies show that mating between transgenic and wild fish is possible,[96,97] just as it is with non-GE farmed fish. The FDA appears satisfied with evidence presented by AquaBounty showing that this would not pose a significant problem given current production locations and methods.[98]

Summary

The issues surrounding genetic engineering are complex and overlapping, rendering most attempts to generalize about GE foods misleading. The abundant information and misinformation on the topic adds complexity to issues ranging from government policy to individual health considerations. This paper has provided information to stimulate informed discussion of the federal government's role in balancing consumer, farmer and industry interests.

Recommended Reading

Center for Science in the Public Interest, "Straight Talk on Genetically Engineered Foods: Answers to Frequently Asked Questions", April 2012, http://cspinet.org/new/pdf/biotech-faq.pdf, accessed 11/5/13.

Jennifer Kuzma & Rachel Haase, "Safety Assessment of Genetically Engineered Foods: US Policy & Current Science," Food Policy Research Center, University of Minnesota, October 2012, http://www.foodpolicy.umn.edu/policy-summaries-and-analyses/genetically-engineered-foods/, accessed 11/5/13.

Nature International Weekly Journal of Science, "GM Crops: Promise and Reality," Nature Special Edition, 5/2/2013, http://www.nature.com/news/specials/gmcrops/index.html, accessed 11/5/13.

Allison Van Eenennaam, Eric Hallerman, & William Muir, "The Science and Regulation of Food from Genetically Engineered Animals," Council for Agricultural Science and Technology (CAST) Commentary QTA2011-2, June 2011, http://www.cast-science.org/download.cfm?PublicationID=21628&File=1e3072cec0393d113f33327f2e2c5a445a5aTR, accessed 12/11/13.

Scientific American, Food Issue, 3 September 2013. Although not available online without a subscription, it is available at libraries and has an excellent series of articles on pertinent food topics, including an article by David Freedman entitled "The Truth about Genetically Modified Food".

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Center for Environmental Risk Assessment (CERA), GM Crop Database, ILSI Research Foundation, Washington D.C., http://cera-gmc.org/index.php?action=gm_crop_database, accessed 11/5/13.

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