GENETICALLY ENGINEERED ORGANISMS (AKA GMOS): ISSUES AND THE SCIENCE

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Genetically engineered organisms (what many call GMOs – genetically modified organisms) are increasingly showing up in newspaper headlines, web sites, blogs, and email. There have been media splashes about new genetically engineered (GE) crop types, proposed labeling legislation, and even shocking photos claiming to show animals harmed by consuming GE crop products. After noting why it may be that genetic engineering has stirred up so much controversy, this article will describe what GE crops are and present information on the risks and benefits associated with this technology. The aim is <u>not</u> to tell anybody what they should think about GE technology, but rather to help explain what is known about GE crops and thus help all of us arrive at better-informed conclusions about this contentious public debate.

WHY THE CONTROVERSY OVER GE CROPS?

It is not often that plant breeding-related topics make it to newspaper covers or are the subject of activists' protests. Why now? Shortly after the first GE crops were commercialized in 1996, Hallman et al. (2001) did a survey of the general public to assess their understanding of traditional crop breeding and the new technology (at that time), genetic engineering. After a simple explanation of traditional cross breeding, respondents were asked "Have you ever eaten a fruit or vegetable created using these methods?" Only 28% correctly answered "yes", while 61% said "no" and another 11% were not sure. Reality is that most Americans have eaten nothing but traditionally cross-bred crops. Responses were very similar when people were asked a question about whether they had ever eaten a genetically engineered fruit or vegetable, despite the fact that almost none were available in the market at the time (Fig. 1). Clearly, the general public has limited understanding of previous human efforts to improve our crop and livestock breeds. Add to that a new genetic intervention with crops that produce the food we eat every day and the fact that some sort of risks are inherent in any new technology, and it is not surprising that concerns emerged.

WHAT ARE GE CROPS?

GE crops cannot be fully understood without first considering the history of our domesticated crops. Virtually all of them had their origins thousands of years ago, with wild species that early hunter-gatherers found to be useful as sources of food. For corn, that wild ancestor was teosinte – a grass with heads containing about ten small seeds that fell on the ground when they were mature and were indigestible unless they were cracked or ground to break open the seed coat. The traits of wild crop ancestors were determined by the genetic code contained in the DNA molecules present in every cell of each plant. That code provides the instructions for how any plant appears and how it grows. The DNA code varies from plant to plant of the same species, allowing for individuals to differ one from another. Since the entire DNA code must be copied every time a cell divides to provide a copy for each daughter cell, copying mistakes (called mutations) happen regularly and they are the source of variation among individuals of the same species.

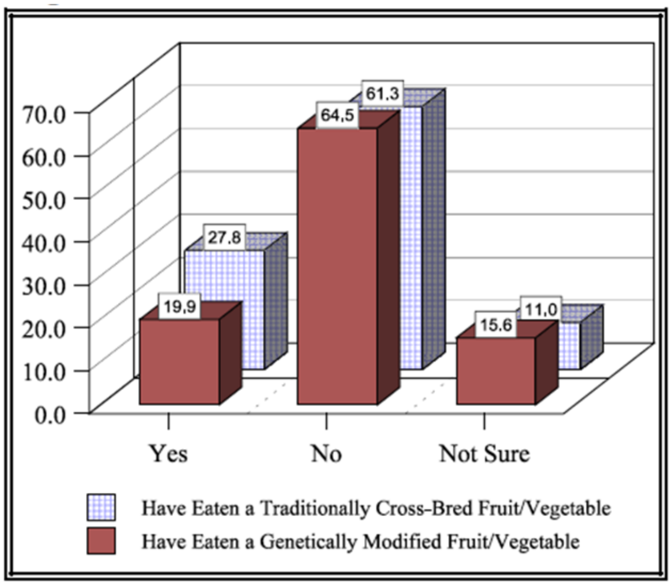

Figure 1. Reported consumption of traditionally crossbred and GM fruits and vegetables. Source: Hallman et al. (2001).

As the early gatherers found naturally occurring mutant types, they collected and saved those that were beneficial to them. For example, they would have chosen and saved teosinte plants that had larger seeds, or seeds that stuck to the central stem (now the cob) when they were mature rather than falling on the ground, or seeds lacking the hard indigestible seed coat. Gradually, those genetic changes (from naturally occurring mutations) combined with farmers' selection of seeds from more useful plants created a new domesticated crop, corn, from what had been a wild plant. That profound change (Fig. 2), which took place in all our domesticated species, was a long-term process of genetic modification brought about by human selection. Since domestication, human breeding and selection of crops and livestock has continued and intensified as our knowledge of genetics and performance measurement has improved. In reality, our domesticated crops and livestock are no longer "natural". Most would never survive in nature (that is, without a partnership with farmers who cultivate or raise them) because they have been so profoundly genetically modified from their wild ancestors.

Genetic engineering is, indeed, a new tool for breeding improved crops. Now that science has allowed us to understand the genes that control inheritance, it is possible to identify the genetic material of an organism that causes it to make a particular product. For example, the bacterium *Bacillus thuringiensis*, long sold as a bacterial insecticide under names like "Thuricide," can infect and kill certain caterpillar-type insects.

Figure 2. Modern corn (left) and its wild ancestor, teosinte (right).

Researchers identified the gene in this bacterium responsible for producing a protein that is converted to a toxin when inside a caterpillar's or beetle's gut. They then cut out this gene (called the Bt gene) from the bacteria and inserted it into crops like corn and cotton to create insect resistant versions of these plants: so-called Bt corn and Bt cotton. For each insect, a slightly different variant of the Bt gene from the bacterium is used because those genes differ in how effective they are against different insect species. In corn, for example, there is a Bt-corn borer gene that is slightly different from the Bt-corn rootworm gene. Both of these genes are built into many commercially available GE corn varieties.

A similar process was used to create GE plants that are able to tolerate being sprayed with herbicides that are normally toxic to plants. These include the glyphosate (Roundup) resistant gene and the glufosinate (Liberty) resistant gene, both originally found in naturally-occurring soil bacteria. Herbicide resistance from these genes (especially the "Roundup Ready" glyphosate resistance trait) has been built into many GE crops, including soybean, corn, cotton, alfalfa, and sugarbeet. Genetically engineered insect resistant (Bt) and herbicide tolerant (HT) crop varieties (including many with both traits together) are planted on the majority of US soybean, field corn, and cotton acres (Fig.3). Clearly these GE varieties have been widely adopted by farmers.

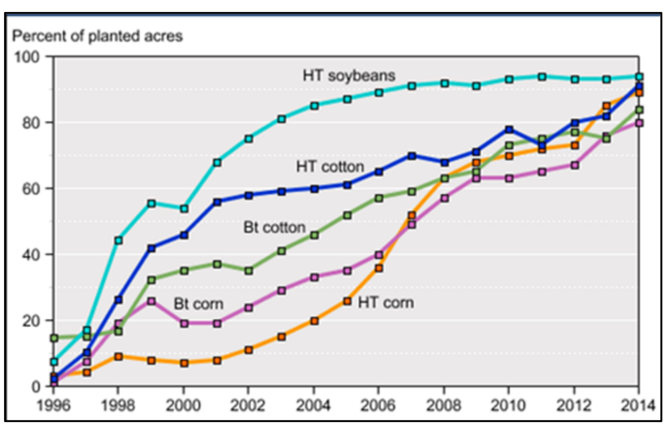

Figure 3. Adoption of genetically engineered crops in the United States, 1996-2014. HT= herbicide tolerant, Bt = insect resistant. Source: USDA ERS (2014).

So how does genetic engineering differ from "traditional" plant breeding? ("Traditional" plant breeding means the kind of selection and breeding practiced by early farmers and by plant breeders up until the 1990s – cross pollinating different parents and searching among the offspring from those crosses to find genetically superior types.) The GE crop varieties now being sold commercially were created by transferring individual genes between organisms that could not naturally cross with each other (like a soybean and a bacterium). For many years, plant breeders have made crosses between crops and their wild and weedy relatives to transfer genes for traits like pest resistance to the domesticated crops, so this process is not entirely new. However, traditional plant breeders are limited to transferring genes between organisms that are so closely related to each other that they can be sexually crossed. A second difference is that in making sexual crosses, the offspring receive a relatively random mix of the genes from both of their parents, and that can include desired genes and any others that come along with them. Genetic engineering inserts only a gene or a few genes into an existing crop variety, so the GE variety differs by only one or a few genes from its parent. Lastly, the ability to identify and manipulate individual genes has led to the legal right to patent genes, so most (if not all) GE traits are patented and their use is legally constrained by the patent holder.

In addition to the differences noted above, there are also similarities between traditional plant breeding and genetic engineering. Both depend on variation or changes in the genetic sequence to create crops that are agriculturally superior. Both approaches aim to modify crops to better meet human needs, just as the earliest farmers who domesticated our crops did. Finally, it is not new that private companies seek a return on their investments in plant breeding. With traditional plant breeding, they were able to do that through plant variety protection laws and through marketing hybrid varieties for which seed must be bought each year. With genetic engineering, the option of patenting genes has provided another avenue for the private sector to seek a return on their investment. Thus, although genetic engineering is a distinct new tool for plant breeding, it shares the same fundamental elements as traditional plant breeding: genetic variation as the basis, improving crops to better meet human needs as the goal, and the need to get a return on research investment in the private sector.

ISSUES AND CONCERNS REGARDING GE CROPS

The issues and concerns being raised regarding GE crops include some that can be informed by science (economics of production and use, environmental risks, food and feed safety) and others that are societal value questions (should GE crop products be labeled in the market, is there too much concentration in the industry that controls and profits from GE traits, is genetic engineering ethically wrong). This section will cover the primary areas of concern about GE crops and describe data and research results that shed light on these concerns.

From a farmers' point of view, the farm-level impacts of growing a GE vs. a non-GE variety is of paramount concern. The National Academy of Sciences' National Research Council conducted a thorough review of peer-reviewed scientific studies that quantified farm-level impact of adopting GE crop varieties (NAS NRC 2010). Although clearly impacts vary from farm to farm due to differences in environment, soils, and production systems and practices, this study reached a number of general conclusions. They found that many farmers had benefited economically from GE crop varieties. Seed of GE varieties is typically more costly because of the "technology fees" for the GE traits, and it is sold with technology use agreements that prohibit saving seed (even for your own on-farm use). There are also some domestic and international markets with limited acceptance of GE varieties. On the positive side, however, GE varieties may have higher yields, reduced labor and production costs, allow greater flexibility in management, and provide increased convenience for producers. In the future, there may be GE crops whose products have value-added benefits for consumers or processors and thus they will receive price premiums, but these types of varieties have yet to be developed and commercialized. What should be clear from this brief list is that economic costs and benefits are very case specific, depending on the individual farm operation, the GE crop and trait being considered, and the marketing environment.

Both farmers and consumers wonder about environmental impacts of GE crops. The NAS NRC (2010) study found, on average, that adoption of GE varieties resulted in positive environmental impacts from reduced insecticide use and less need for tillage (resulting in reduced erosion potential). For example, Figure 4 shows the reduction in insecticide use in field corn that has occurred with increased adoption of Bt corn varieties. The results regarding herbicide use were less clear: overall herbicide use increased with adoption of GE crop varieties, but there was more use of an herbicide generally considered to be less toxic (glyphosate) and reduced use of some of the more environmentally undesirable herbicides. Figure 5 shows herbicide data for cotton, where the increase in total herbicide use can be seen, and for soybean, where the shift in types of herbicides used is most pronounced. This combination of changes makes debate regarding herbicide use particularly complicated: opponents of GE crops can point to data showing that increased GE crop adoption has resulted in increased herbicide use, and advocates of GE crops can point to data showing that more environmentally-friendly herbicides are being used and reduced tillage (with its environmental benefits) has been promoted. Both points are correct, but neither provides the full picture.

The NAS NRC (2010) study noted the risk from pest evolution to overcome GE resistance. This is a risk for any pest control method, including traditionally bred resistance, chemical pesticides, and even some cultural control methods. Evolution of pest resistance to a control measure happens most readily when a single control approach is used repeatedly and over a large acreage. That is exactly what is happening with glyphosate resistant crops, and farmers are beginning to see weeds that are resistant to glyphosate. There is evidence of the same problem with corn carrying the Bt-corn rootworm trait, and a few well-documented examples of control failures have occurred in recent years (e.g., Gassmann et al. 2011). Both GE crop types have been very popular and provided very good pest control. Their effectiveness may have led farmers and the seed industry to overuse these approaches. As with any pest control measure, overuse favors pest evolution towards more resistance. The importance of rotating or alternating pest control methods is a principle we learned long ago and have promoted through integrated pest management programs. It seems we need to re-learn it with respect to GE pest resistance tools!

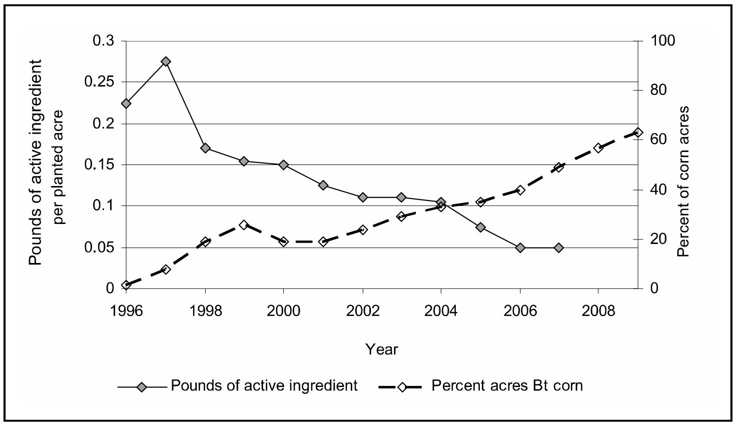

Figure 4. Insecticide use on field corn (solid line) and adoption of Bt insect resistant field corn varieties (dashed line) in the U.S. from 1996 through 2007. Source: NAS-NRC (2010).

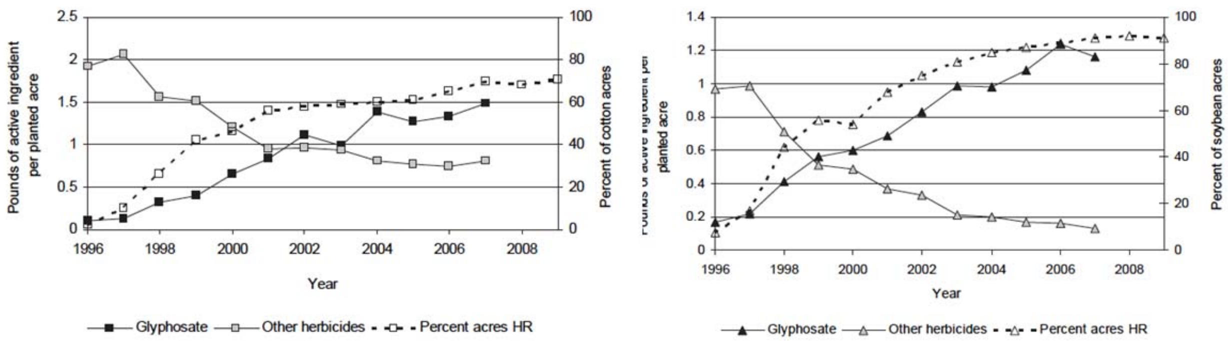

Figure 5. Herbicide use on cotton (left) and soybean (right) in the U.S. between 1996 and 2007. Solid black line: glyphosate use, solid gray line: other herbicide use, dashed line: percentage of U.S. acres planted to GE herbicide tolerant varieties. NOTE: The strong correlation between increased acreage of herbicide tolerant varieties and changes in herbicide use suggests, but does not confirm causation between these variables. Source: NAS NRC (2010).

From a consumer's point of view, the logical concerns are whether GE crop varieties are found in foods, whether they are safe as food and feed, and whether GE approaches have or could introduce allergens into common foods. Food safety testing of GE crops in the US is based on a principal called "substantial equivalence." Under this approach, the new protein being produced by a GE variety (for example the protein that detoxifies the herbicide glyphosate or the Bt protein that provides insect resistance) is tested just as any other new food additive, preservative, or pesticide residue would be tested. The GE protein must be found to be safe and non-allergenic at levels well beyond those found in food and feed. This safety testing is mandatory.

In addition to testing the new GE protein, the overall nutritional composition of the GE variety is compared to see if it falls within the range of normal variation for non-GE varieties of the crop. If so, the GE variety is considered substantially equivalent to non-GE varieties and food safety testing of the whole crop product is voluntary. This approach does not sound particularly reassuring to concerned consumers. The problem is that toxicological safety testing (like that conducted on food additives, pesticide residues, new GE proteins, etc.) done on whole foods would reveal a variety of natural toxicants and/or anti-nutritional substances in the non-GE foods that we have all eaten and accepted as safe for decades. That is because toxicology tests are based on offering a high dose of a food or ingredient to a laboratory organism over a very short period of time. That is not how we consume our foods in a normal diet, of course, so negative effects are not surprising. There are no really good laboratory-based tests that can be conducted in a reasonable amount of time to assess safety in a system that mimics how we actually consume food: in a mixed diet of many different foods each eaten in small amounts over a long period of time. Consequently, the US uses substantial equivalence to assess food and feed safety of GE crops, and stipulates that a new GE variety should be as safe as traditional varieties that we have consumed over time. Food and feed safety testing is required in those cases where a product is not "substantially equivalent" to its non-GE counterpart – a requirement that has not been triggered by any of the currently commercialized GE crop varieties.

Much media attention has focused on the dietary safety of GE crop varieties and whether the US approach for assessing this is adequate. A body of over 100 independently-funded studies has not revealed evidence of any food or feed safety concerns with currently-commercialized GE crop varieties. Those few studies that have purported to show problems from feeding GE crops have been very widely discredited by experienced scientists for their poor design, inappropriate analysis, and other scientific problems. There are also many peer-reviewed, published studies conducted by the private sector that show no evidence of food or feed safety concerns. Some people regard these studies as suspect, since they have been done by the same companies who have a vested interest in marketing the GE crop seed. That is true, but two points should be taken into account. First, these studies have had to meet the same standards of scientific scrutiny that the peer-reviewed publication process demands, which provides some assurance of scientific integrity. Secondly, it is not clear that any entity is willing to pay for extensive safety testing to be done in the public sector (on the contrary, public funding for research has long been on the decline). In the absence of public funding, testing is left to those who can hope to recoup their research investment – the private sector companies who hope to market GE seed.

Concern about novel and unanticipated allergens is also important for consumers, as there is the chance that genes from organisms we don't normally consume as food might have allergenic potential. Testing for allergens has relied on scientific understanding of the general nature of allergenic compounds, and on evaluating how fast the new proteins produced by GE varieties break down in human digestive enzymes. New gene products that are anything like known allergens are extensively tested. Any new protein that breaks down more slowly than others when exposed to digestive enzymes is extensively tested (the longer something stays in your stomach without breaking down, the more time it has to cause an allergic reaction). Again, this scientifically sound approach to monitoring for allergens has not proven very reassuring to concerned consumers, but it is not clear that a better approach exists.

There are other areas of concern about GE crops that are not scientific in nature. These concerns include the debate about labeling GE-derived foods, concerns revolving around consolidation of seed industries and profits from GE crops, and opposition to genetic engineering that is ethically or religiously based. As noted at the beginning of this section, there is a limited contribution that science can make to these debates. However, the following paragraphs provide some data in which to ground discussions of these concerns.

At present, there is extensive political and media debate about whether foods derived from GE crop varieties should be labeled. Various groups have estimated that 60% to 70% of packaged foods in a typical U.S. grocery store contain one or more ingredients from a GE crop variety. This level is not too surprising given the prevalence of ingredients derived from corn and soybean (and even cotton) in our processed foods, and the fact that over 90% of U.S. acreage of these crops is planted to GE varieties.

Most food labeling in the U.S. is product based: it tells something about the content of the food in the package (how much protein, fat, oil, fiber, vitamins, etc. is in a serving). However, many of the corn, soybean, and cotton derivatives found in processed food are highly refined ingredients, like corn starch, oils, corn syrup, soy lecithin, and many more. These ingredients are purified and they do not contain any DNA or proteins. In such highly refined and purified ingredients, there will be no detectable difference between a version derived from a GE variety and a version of that same ingredient derived from a non-GE variety. For example, corn syrup is chemically just sugars and water, so corn syrup from a GE corn and corn syrup from a non-GE corn will be chemically identical. This complicates labeling, because packaged foods that contain these highly refined ingredients from GE varieties would show no measurable difference from those made with ingredients from non-GE varieties, raising the question of what the label tells us and the complication that there is no means for verifying the accuracy of the label.

A consumer survey that asked “Should GM food be required to be labeled?” found that 73% of respondents said “yes” (Hallman et al. 2013). That same survey asked “What information would you like to see on food labels that is not already there?” and only 7% of respondents brought up GE crop content. As always, the answer you get regarding the importance of labeling to consumers depends on how you ask the question. Proponents and opponents of labeling will use different parts of this same study to make their case – clearly an over-simplification of what the data tells us. There is no doubt that labeling will imply a cost (primarily due to keeping GE and non-GE crops and their products separate form planting to the grocery store shelf, and tracking them to assure label accuracy). It is not clear that labeling will increase consumer choice, since there are already non-GE options available in stores (including both certified organic products, which cannot contain GE-derived ingredients, and products voluntarily labeled as “GMO free”).

There is some concern that GE crops contribute to the overall trend toward consolidation, globalization, and industrialization in agriculture. The ability to patent genes appears to vest control over the raw material of agriculture – the genetics of our crops and livestock – in large private sector corporations. Developing and bringing a GE crop variety to market is a costly prospect, so it is beyond the reach of many smaller seed and crop breeding enterprises. Recovering the research and development investment for GE varieties has led some seed companies to seek as many outlets for their varieties as possible, adding additional push to what was an on-going trend toward consolidation in the seed industry. This can be seen by examining which companies have received approvals to commercialize GE varieties, and who now owns those companies. Of the 100 approvals for GE variety commercialization that have been granted in the U.S. to date, the original applicants included 28 different entities (private companies, universities, government agencies; Fig. 6, left). With industry consolidation that has taken place since approvals were granted, these now represent only 16 independent entities, and 80 of the 100 GE variety approvals are held by only four seed companies (Fig. 6, right). Whether this degree of concentration in ownership of GE crop technology is cause for concern is a societal value judgment, not a scientific question.

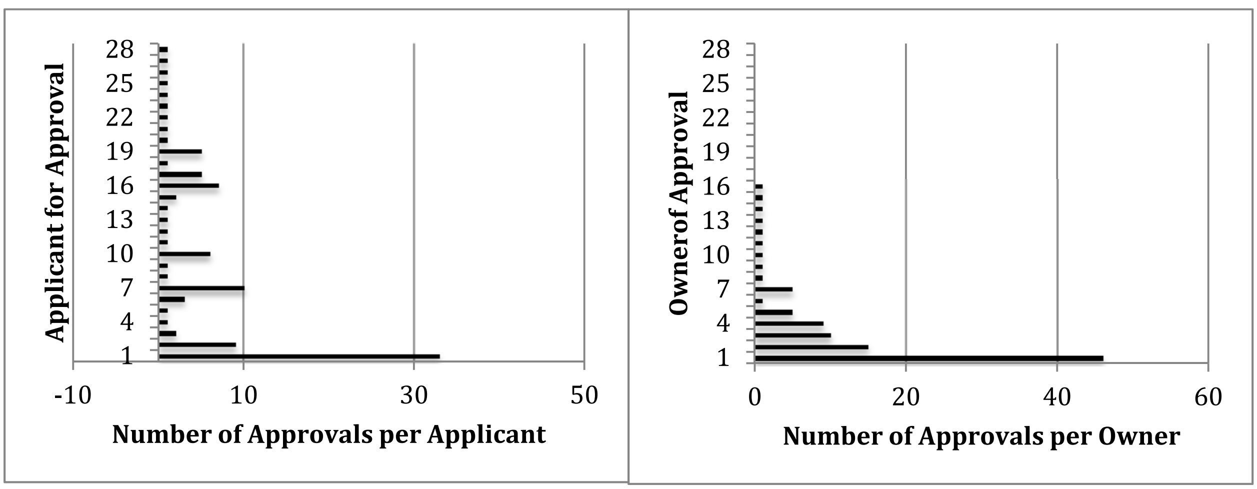

Figure 6. Original applicants for approvals to commercialize GE crop varieties (left) and owners of those permissions after seed industry consolidation (right). Data source: ISB (2013).

Some oppose GE technology based on ethical or religious beliefs. These too are concerns that cannot be answered by scientific studies. They will have to be addressed through policy-making and regulation, which are the approaches we use to implement societal value judgments.

SUMMARY

So what's the bottom line? GE crop varieties have their basis in genetic variation and creating new genetic combinations – approaches we've used for centuries to improve our crops for human use. However, GE is a new and different tool for crop improvement. The resulting varieties need to be monitored for their effectiveness, safety, and environmental impacts just like any other new technology. The outcomes of such evaluations will vary depending on the particular crop and trait, so evaluations must be made on a case-by-case basis. The currently commercialized GE varieties, which are primarily (but not exclusively) corn, soybean, and cotton varieties, have proven themselves attractive to farmers and have not revealed any negative effects as food/feed. They have reminded us what we should have learned well a long time ago – it is unwise to repeatedly use the same pest control methods over large areas, because the pests tend to evolve to overcome those control methods. So we all need to remember that GE varieties, just like any other technology, are not a silver bullet. They must be used wisely.

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