

Understanding risk and safety assessment for genetically modified plants

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When we speak of acceptability of products of genetic engineering, our language is often infused with the terms risk and safety. Concepts of risk and safety are in fact very important for the ways by which we decide to accept and use a given genetically modified (GM) plant or, for that matter, any technology. And the application of these concepts is central to the way regulators and scientists make determinations regarding the acceptability of a particular product of genetic engineering through the process of risk (or safety) assessment. In order to describe the process by which risk assessments are performed and evaluated, we need to first understand the juxtaposition of the terms risk and safety.

Risk and Safety

In everyday use we tend to think of risk as the complement of safety; as in the notion of that which is not safe, is a risk. The relationship of risk to safety is in fact much more complex.

The complexity in dealing with risk and safety arises largely because the general public understands risk as a mixture of what we know, whom we trust, and what we perceive. When first encountering new technologies, the inclination by the general public is to view risks largely on the basis of perception since public knowledge may be limited and trusted experts may not be readily recognized. Furthermore, risk perception is largely driven by a balance of emotive factors such as uncertainty, dread, fairness, control, and benefit, which tend to skew estimates of risk. One consequence is a tendency to overweight risk from an unfamiliar source where exposure seems outside of our control and where the personal benefit may not be clear (a chemical residue in food), while minimizing risk associated with something familiar and useful in our everyday lives which we feel we control (automobile travel).

In order to limit perceptions as a basis for understanding risk, risk is formally considered by experts through an objective, science-based activity known as risk assessment, which is designed to focus on what is known on the basis of evidence and thus minimizes what we as individuals might feel on the basis of perception. The use of a formal approach for risk assessment helps analysts to lower their personal viewpoint, so as to limit the intrusion of perceptions into considerations of risk.

With respect to GM plants, risk analysts mostly use the term risk to describe the likelihood that there will be an undesired consequence or harm under the conditions by which we encounter the GM plant in our environment. If the analysts were able to undertake risk assessment in a fully

quantitative sense, which is frequently not possible, the risk could be described as a conditional probability arising from exposure to the GM plant and the adverse consequence that would arise from that exposure. More frequently the risk is described as a likelihood or degree of concern based on an understanding of the GM plant itself and a comparison to similar non-GM plants with which we are familiar. Regardless of whether we describe risk with quantitative exactness as a probability (ranging from zero to one), or in the more general context of a likelihood, we are faced with the fact that whenever or wherever we encounter anything in our lives there is some degree of risk (risk is zero only in the absolute absence of exposure).

When we speak of a comparison of the GM plant to something with which we are familiar, we begin to invoke precepts of safety. We tend to describe something as safe when we judge its risks to be acceptable. Because safety is a judgment, it is value laden; so, that which we describe as safe will be understood within contexts of society, culture, politics, and economics. The upshot of this is that if risks are assessed by the same process and with the same underlying base of knowledge, the likely (or probable) risk will always be similar for a given case — but the safety will not, since it will incorporate subjective judgments of the risk relative to experience, benefits, and socio-cultural contexts.

So, in the best of circumstances we could hope to achieve the same (harmonized) processes for risk assessment regardless of where they are conducted. And with the exception of the somewhat different ways questions of risk may be formulated from one place to another, we would expect the same or very similar answers to “What is the risk?” when the same or similar cases of risk assessment are undertaken. That is, we would expect various lines of evidence in the conduct of risk assessments to point to similar conclusions regarding the nature and magnitude of risks. We would never expect, however, that from place to place throughout the world that a given level of risk would be uniformly deemed safe, since that determination will reflect differing norms of acceptability of risk depending on where and by whom the consideration is made.

Food Safety Assessment

Against this backdrop of risk, safety, and their interrelationship, consider a particular instance of risk assessment for a GM plant — safety for food use of corn genetically engineered to be resistant to insect pests. The risk analyst first proceeds from an understanding of safety as reflected in comparability through a hypothesis that other than for the intended change brought about by genetic engineering, the GM corn is familiar and equivalent to corn as we know and use it. This comparison is made because we recognize that corn as we know and use it is familiar and safe. Note that stating that we recognize non-GM corn to be safe does not mean it is risk free, since for some minor portion of the population corn may pose a health risk due to components to which they are allergic. We say the non-GM corn is safe because we accept the degree of risk it poses. This determination of safety can be done in various ways, but for plants such as corn with which we have long familiarity as a food source, we typically say the plant is generally recognized as safe simply on the basis of societal experience.

In undertaking this comparative determination, the risk analyst will account for the history, use, and spectrum of composition (phenotypes) of corn as it is grown, processed, and consumed. Juxtaposed on this is a consideration of the way the corn has been transformed by genetic

engineering — Where has the new genetic element been inserted in the genome? And how stable is the gene and its product over generations and across environments? How does the composition of the GM corn differ from other corn in ways that are important to the growing, processing, and consumption of corn, such as in its contents of nutrients, antinutrients, or food toxins? Through this scheme of comparability, the risk analyst is able to address the hypothesis of familiarity and equivalence to corn as we know and use it and recognize it to be safe. Answering this hypothesis in the affirmative leaves the risk analyst with a focused consideration for further risk assessment — This is, does the change in corn that has been manifested by genetic engineering pose a risk in food?

Risk assessment focused on the change brought about by genetic engineering allows for detailed consideration of the potential consequences of the change relative to the way the GM plant is intended to be used and the environments in which it may be found. Continuing with our example of safety for food use of corn engineered to be resistant to insect pests, the risk analyst at this stage can ask how specifically the change manifested by genetic transformation — expression of an active protein conferring insect resistance to the plant — may pose risks to consumers of food derived from the GM corn. In terms of potential food safety, key considerations are how the change may result in toxicity or allergenicity.

Toxicity is the capacity or property of a substance to cause adverse effects. For proteins — the changed component in our example is a transgenic protein that is now expressed in the plant — acute (that is high dose, short duration) exposures are good indicators of toxicity. Maximum-limit dose studies using the purified protein (that is the changed component of transformation to create the GM plant) expose test animals to the highest concentration of the protein that can be administered with the test system used. Since this test results in doses many times higher than would be possible from the protein in food, absence of a toxic response in this study with purified protein indicates that an acute exposure to the protein in food would not be considered a hazard in foods and there is reasonable certainty of no harm.

For proteins, a finding of no harm in acute studies is generally understood to indicate reasonable certainty of no harm from longer-term exposures at lower, more realistic concentrations as well. This is frequently confirmed in longer-term feeding studies in which test animals receive the transgenic food as a major component of their daily diet over periods of up to 90 days. Depending on the test animals used for these studies, the proportion of transgenic food in the diet may range from 25 percent (in mice or rats) up to 60 percent (chickens) of total dietary intake. A differing nature of change brought about through the genetic engineering of plants may result in differing responses in toxicity testing then for this example, in which case a more refined regime of toxicity testing may be deemed appropriate by the risk analyst. The specific testing and further assessment required would be consistent with established paradigms for demonstration that a food may be generally recognized as safe.

A specific aspect of food safety that is especially important for foods is that of allergenicity (see article by Chassy 2008). Allergenicity is an immune response to sensitization to foods or other stressors that we encounter in our environment. Testing foods for allergenicity is complicated by the lack of useful animal models; therefore, when risk analysts consider a protein transgenically expressed in plants, they use a line of evidence that considers characteristics of

proteins known to be allergens. The screening-level assessment considers whether the protein comes from a source known to be allergenic, if the amino acid sequence is similar to that of known allergens, and whether the protein will be stable under conditions simulating digestion in the human gut. If the answer is yes to one or more of these, there is a need to undertake more advanced considerations such as serum cross-reactivity or animal tests (if a reliable test is available).

Because of uncertainties surrounding safety assessment for allergenicity, the more general outcome if a transgenic protein is found to have one or more attributes of an allergen is for the GM plant not to be developed as a food. Thus, any GM-plant-derived food approved for cultivation or importation will not have attributes generally associated with known or putative allergens. A somewhat similar screening for protein toxins may also be performed as a precursor to toxicity testing. Note that the safety-assessment approaches that are used for allergenicity and protein toxicity follow the paradigm of comparability by likening the attributes of the GM plant (or more specifically the expressed product) with those of similar products with which we are familiar.

The understanding of GM-plant food safety and toxicity is often corroborated by animal performance testing. These studies are intended to ensure that GM plants and their products are suitable (and perhaps superior) feed sources for production animals for purposes of product marketing. Proper animal performance when fed the GM source provides indirect evidence of food safety and thus adds to the lines of evidence approach for safety and risk assessment.

Environmental Risk Assessment

Environmental risk assessment (ERA) considers the impact of introducing a GM plant into a given environment. The ERA is concerned with evaluating the potential for harm to ecosystem components given that there is exposure to the GM plant. Importantly, the focus and degree of emphasis on elements of the environmental risk assessment will change during the development process for the GM plant as the scope of environmental release ranges from confined field trials of limited extent through to larger-scale trials and seed increases in more environments, and to the final unconfined commercial release.

The ERA for a GM plant follows the same basic approach as for food-safety assessments; that is, the assessment is conducted on a case-by-case basis, is comparative, and uses lines of evidence to arrive at a holistic understanding of the nature and degree of risk posed by the particular type of environmental release being analyzed. In addition, a stepwise or tiered approach to data generation and analysis is used in order that the focus is directed to consequential concerns within the universe of possibilities.

Because the universe of possible concerns relevant to environmental risk assessment is very large, the process of problem formulation is especially critical in order that the risk assessment be properly framed and conducted. The universe of concerns generally boils down to a few very specific questions that need to be addressed in the ERA for most GM plants: Does the modification of the plant cause it to have attributes commonly associated with weeds in managed environments? Invasiveness in natural environments? Will the transgenic element in the GM

plant move into native plant populations (gene flow — see article by Stewart 2008). And so what if it does? That is, will gene flow cause a native plant to become weedy or invasive (or more so)? Or will isolated populations become extinct through hybridization with the GM plant (gene swamping)? And will the GM plant adversely impact non-target organisms that may be of special interest because they are beneficial, endangered, threatened, or charismatic? Problem formulation is a formal process whereby the risk assessor determines relevant considerations for risk assessment from this wide host of possible concerns.

The commercial development of a GM plant proceeds in a stepwise fashion and environmental release in the first instance is in the form of field trials that are limited in number, size, and environments in which they occur. As development continues, the scale of release is larger in terms of size of plantings, and there is a lessened degree of confinement. Thus, for example, in later stages of development seed increases may mean the plant occurs on many thousands of acres with few conditions for confinement. Finally, with commercialization the GM plant is widely deployed with little concern for its confinement. Obviously, the nature of environmental impacts that need to be addressed, and therefore the data intensity and degree of scrutiny given these impacts in the ERA, will vary with the stage of development and scale of deployment being considered.

In view of this, the environmental risk assessment proceeds in a tiered fashion where the problem formulation considers the specific questions to be addressed and arrives at relevant data and data synthesis needed to undertake the appropriate ERA. The ERA is therefore dynamic with respect to the questions addressed, the data synthesized, and the comprehensiveness of the analysis conducted. As the environmental risk assessment iterates through tiers, conservatism in conduct and interpretation of findings is balanced against uncertainties in the state of understanding — thus, lower-tier ERA will be highly conservative to balance uncertainty and, as higher tiers of assessment are needed, increased understanding allows for more realistic (less conservative) appraisals.

Other Types of Risks

Economic costs of adventitious occurrence. Economic risk unrelated to human health or environmental concerns is a frequent consideration of importance relative to the acceptance and use of GM plants. The most prevalent economic costs (i.e., risks) are from transgenic elements out of place. This means evidence for the unintended (adventitious) presence of transgenic elements (trait presence, that is, the detection of genes, gene fragments, or expressed products from GM plants). Examples are when trait presence occurs in organic foods (where certification standards do not allow intentional presence), in other food items that are marketed as GMO-free, or in imported commodities where import approvals for a specific trait are not in place.

Adventitious occurrence can lead to local, regional, or international disruptions of food distribution systems that result in both direct and indirect costs throughout the food supply. While risk assessment can help to determine the costs associated with such disruptions, they are usually meaningful only in the retrospective sense — as a way of analyzing for the source and extent of unintended occurrence once it has been recognized.

One aspect of risk assessment which is helpful in reducing the incidence of unintended trait presence is confinement analysis which evaluates the effectiveness of various means for confining and channeling GM traits and their distribution in seeds, foods, and feeds. In commercial crop production, confinement measures are used by those who have different standards than the market standard. For instance, in the U.S. the organic farmer takes special measures to limit occurrence of GM traits; the neighbor who produces a GM plant is not mandated to change his or her practices to accommodate the organic farmer. Confinement analysis allows for effective risk management actions — such as buffer zones, temporal planting offsets, equipment clean-out procedures, and auditing procedures — which can reduce the incidence of unintended trait occurrence.

Resistance management. Resistance management is the activity related to assuring continued availability of plant protection products. For instance, insect-resistant (IR) plants will lose efficacy if the insects targeted for control become resistant to the protein toxins expressed by the IR plant (see article by Shelton 2008). Similarly, herbicide-resistant (HR) plants are used in conjunction with herbicides for which the plant is resistant to allow for safe and effective control of a broad spectrum of weeds. Misuse or overuse of this technology may lead to the development of weeds resistant to the herbicide and therefore diminish the value of weed control strategies based on the herbicide-HR plant combination.

Risk assessment is used to determine what types of management practices and courses of remedial action will be most effective in retaining the efficacy of these products.

Risk Findings and Decision-Making

Risk assessment is an outgrowth of the need for regulators to make sound, science-based decisions regarding the risks and safety of technologies. Genetically modified plants represent a valued technology that can provide societal benefits in terms of reduced exposures of chemical toxins to workers as well as in foods and the environment; lowered costs of production; increased ease of plant management decision-making; and a reduced environmental footprint from agricultural practices (such as through improved chemical use and reduced soil erosion).

These benefits must be balanced against possible costs (risks) of the technology. Risk analysts are involved in the assessment, management, and communication of risks and within democratic societies are vested with responsibility to aid in societal decision-making through a balanced consideration of risk versus benefit. For GM plants there has been a steady improvement in the formal processes by which the risks of their production and use can be objectively evaluated for the purpose of decision-making.

Although risks of GM plants can be objectively evaluated through the formal process of risk assessment, the judgment as to the acceptability of risk (that is, safety determinations) is value-laden, and this reflects subjective societal opinion regarding the desire to use any given technology. To date, commercialization and widespread adoption of GM plants has been possible due to a rigorous risk- and safety-assessment process which has shown reasonable certainty of no harm to human health and the environment.

For Further Reading

- A primer on the regulatory process for food and environmental safety assessment of GM plants with in the U.S. can be found at <http://www.bigmap.iastate.edu/modules/>.
- Chassy B. 2008. Food Safety of Crops and Foods Produced Through Biotechnology. <http://agribiotech.info/Chassy%20-%20Food%20Safe%20March%208%20-%202003.pdf>.
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