

---

## Risk assessment and regulation of bioengineered food products

---

Sheldon Krinsky

Department of Urban & Environmental Policy, Tufts University,  
Medford, MA 02155, USA

Fax: +1-617-627-3377 E-mail: skrimsky@emerald.tufts.edu

**Abstract:** Europe is the epicentre of what has been described as an all out war over the acceptance of genetically engineered foods. Controversy over health effects has centred around simple and complex models of transgenic modifications. Proponents of the simple models emphasize familiarity with the host plant and the well-characterization of the transgene. Advocates of the complex models consider the genome to be more like an ecosystem than a set of Legos. They emphasize the indeterminacy and unintended outcomes of foreign gene insertions. Evolving concepts of health that embrace health promotion and sustainable agriculture set additional standards for transgenic crops that transcend reductionist approaches to risk assessment based on contested genomic principles.

**Keywords:** Biotechnology; genetically engineered foods; bioengineered; health effects; transgenic modifications; genome; agriculture; transgenic crops; genetically modified; substantial equivalence; allergens.

**Reference** to this paper should be made as follows: Krinsky, S. (2000) 'Risk assessment and regulation of bioengineered food products', *Int. J. Biotechnology*, Vol. 2, Nos. 1/2/3, pp.231–238.

**Biographical notes:** Sheldon Krinsky is a Professor in the Department of Urban and Environmental Policy at Tufts University and adjunct professor in the Department of Family Medicine and Community Health, Tufts Medical School. He is co-author of *Agricultural Biotechnology and the Environment* and author of a new book titled *Hormonal Chaos: The Scientific and Social Origins of the Environmental Endocrine Hypothesis*.

---

### 1 Introduction

Rarely, in the modern history of technological risk, has there been a global debate of such intensity and polarization on a subject for which there is such a dearth of definitive knowledge, so much conjecture, and so little mutual understanding. That is the state of affairs of bioengineered plants, food and micro-organisms. We are not dealing with a single product like DDT, or chemical groups like dioxins or PCBs but with a new process for modifying crops. Some have argued that we should be regulating products, not processes. After all, from the point of view of the safety of the molecule, do we care how we manufacture PCBs? The toxicological properties of the 200 plus congeners comprising this chemical family are what are important and not how they are made. Why don't we address the health effects of bioengineered plants like we do chemicals such as

PCBs? If we can get to the root of this question, we may be able to understand more fully the nature of the current debates.

I shall make three summary points. First, there are no canonical tests to evaluate crops that have been genetically modified. This is unlike the situation of assessing chemical risks where industrialized societies have had 50 years to develop testing mechanisms and to identify precise chemical structures. Each transgenic crop has to be examined on its own terms for its nutritional qualities, allergenicity, toxicity, pathogenicity, pleiotropic, and ecological effects. The tests for transgenic crops are being invented as the products move off the assembly line. The country that hosts the greatest number of products developed by genetic technology, namely the United States, does not have standards in place for testing these products or laws in place for regulating their entrance into the marketplace. Second, the concept of health is evolving and with it so are the expectations for evaluating new biotechnology food products. The term healthy foods has come to mean more than foods that do not produce acute toxicity. Nutritional health, and the health of the food production system, including the animals and the soil have become part of a new vision of sustainable agriculture. And third, the health concerns of genetically modified food are intertwined with other factors of public interest including agroecology, structure of farming, seed oligopoly, and international truck. Thus, the health risks are embedded in national and international truck and environment concerns and may serve as a proxy for issues that are not obvious or transparent.

## **2 Modes of discourse: of legos and ecosystems**

There are three primary modes of discourse in the debate over genetically modified crops/food: human health; ecology; socio-economic. Under human health the focus is on the quality of the food product. Will transgenic food spread allergens, introduce toxins, or change the nutritional composition of the products? The ecological discourse includes concerns about the impacts of transgenic organisms on non-target species and the contribution of bioengineered organisms to sustainable agriculture. Will the modified organism narrow biodiversity, transfer their genes to other organisms, or behave like non-indigenous introductions? If genetic engineering can endow plants with water or salt tolerance, is that analogous to introducing desert plants into environments with plentiful rainfall or to expanding the weeds that survive in brackish soils? And if so, what will the ecological effects be? Can GM plants escape the biotic and abiotic factors that normally constrain them from becoming pests?

The discourse on genetically modified plants/foods (GM crops) includes concerns about the socio-economic effects of introducing these products into commerce. What is the role biotechnology plays in the control of agricultural inputs to farming, in the autonomy of farmers, or in the rate of decline of the family farm? Within these discourses, parties in dispute offer distinct scientific and policy frames that define and characterize the issues.

In the contested issues over GM crops, the context of the innovations plays a key role in how the protagonists and antagonists construct their realities. Critics seek to evaluate new products in the broadest context where there is still considerable uncertainty, while proponents seek to delineate the context to issues for which there is a comfortable scientific consensus.

Within the various discourses, two models of GM crop health risks, which I shall refer to as the simple and complex models, distinguish sceptics from promoters of the new transgenic food products. These differences are rooted in the epistemology of genomics: what scientists believe they know and can predict about the genetic alteration of the plant genome.

In the simple model, familiarity with the parental plant and the well-characterization of a gene whose protein product is not known to be harmful to animals or humans would qualify the GM crops as safe for human consumption. The simple model sees no important distinction between rDNA techniques and other methods of altering the genetics of plants. The source of this contention can be traced back to a report issued by the National Academy of Sciences in 1989. According to the study "crops modified by molecular methods in the foreseeable future pose no risks significantly different from those that have been accepted for decades in conventional breeding" [1]. As a consequence, no special regulations are deemed necessary. A product that meets a short list of requirements is acceptable. In the United States, genetic modification of plants is seen as one of several ways to create new varieties and because of the extensive history of safety of plant varieties developed through agricultural research, the US Food and Drug Administration (US FDA) has not found it necessary to review the safety of foods derived from new plant varieties [2]. The term substantial equivalence has been introduced into policy frameworks to characterize a GM food product that is presumed to be essentially equivalent to its natural antecedent (or parental crop) and thus poses no new health risks. Millstone *et al.* consider substantial equivalence a pseudo-scientific concept masquerading as if it were scientific [3]. The authors are correct: without agreed-upon criteria, the reasoning given for substantial equivalence is circular.

The complex model of the plant genome looks at multiple pathways of gene expression and pleiotropic effects – introduced genes may affect the expression of other genes in the parental plant, thereby increasing toxicity of food components [4]. Some scientists argue that the health assessment of GM crops must take account of the positioning effect of transgenes. Since we cannot predict the position of the foreign gene within the plant's genome, we will not be able to determine what other gene expressions or suppressions will take place [5]. In the complex model, the gene system is contrasted with the child's game of Legos, where insertions do not affect the other elements of the system. According to Mae-Wan Ho [6]:

"Because no gene ever functions in isolation, there will almost always be unexpected and unintended side-effects from the gene or genes transferred into an organism".

Two transgenic lines of a crop produced from the same gene insertion, grown under the same conditions, may yield different quantities of a protein based on the positioning of the transgene. The possible risks cited by those who advocate the Lego model of the plant genome visualize a broad range of health and ecological risks.

A British scientist who discovered that a transgenic potato fed to rats resulted in immune damage commented:

"These positioning effects are not simple to predict. Think of William Tell shooting an arrow at a target. Now put a blindfold on the man doing the shooting and that's the reality of the genetic engineer when he's doing a gene insertion. He has no idea where the transgene will land in the recipient genome" [7].

Compare these views on plant genetics with the following statement of members of the US FDA:

“...any single gene trait (and, potentially, multi-gene trait) whose chromosomal location or molecular identity is known can be transferred to another organism irrespective of mating barriers...without simultaneously introducing undesirable traits that are chromosomally linked to the desirable trait in the donor organisms.”

Thus, according to the official US FDA position the rDNA techniques have great power and precision [8]. In contrast, a scientist from DuPont’s advanced research facility for plant-based materials was quoted: “No one really understands how to control and regulate plant gene expression” [9]. Those backing the more complex (ecosystem) model of the plant genome call for clinical-trial type experiments with human volunteers. They use the drug model as the paradigm for GM crops. The drug model operates under the precautionary principle: every new drug is guilty until proven innocent.

Once a foreign genes is transferred to a crop, a company selects from hundreds or thousands of plants those with a stable transgene in the proper location that provides the trait of interest. Some of the uncertainty may be reduced by the selection of multi-generational progeny to insure stability. But the stability of the transgene, which is critical to the economic viability of the plant, is only one consideration of its safety. We must also understand how the transgene interacts with other elements in the genome – a consideration often neglected in the Lego model.

Also, when a desired gene is incorporated into a plant, there are usually other genes present. Among them are antibiotic resistant markers. Will these markers compromise the use of antibiotics to treat human pathogens? What type of evidence is required and what types of tests can insure the safety of consumers? Proponents and opponents of GM crops are divided on this issue. The US FDA considers the transfer of an antibiotic resistance marker from plants to micro-organisms in the gut or in the environment to be a remote possibility with insignificant outcomes when compared to the natural transfers of resistance genes between micro-organisms that take place. However, the US FDA leaves it up to the seed developers to evaluate the use of antibiotic resistance marker genes in crops on a case by case basis. The agency issued a guidance document which states that such markers should not be used in food if it could compromise the use of clinical antibiotics, such as when a particular antibiotic is the only drug available to treat a clinical condition. The guidance document does not create or confer any rights for or on any person and does not operate to bind US FDA or the public; it is strictly a guidance to industry [10].

Other genes transferred to plants are promoters that may be part of the vector system used to transport the desired gene. Examples include plant viruses that are used to switch on the gene once it has been transplanted into the plant. Thus, the Cauliflower Mosaic Virus (CaMV) is used to switch on the lectin gene in potatoes. Will these promoter genes create other gene products? Sceptics emphasize how imprecise the process is while proponents applaud the precision compared to traditional hybridization of crops. The science is barely able to keep up with the commercial developments. In a recent article in the journal of *Microbial Ecology in Health & Disease*, the authors warn that a promoter sequence in CaMV (a sequence of about 350 basepairs) is functional in other organisms indicating that recombination of the CaMV promoter elements with dormant, endogenous viruses may create new infectious viruses in all species into which the transgenic DNA is transferred [11]. They argue that the transgenic crops containing CaMV 35s or similar

promoters should be withdrawn from sale and from use for human consumption or animal food.

Barry Commoner, trained in molecular biology and a critic of its reductionist formulations, asks whether science is ready for large scale applications of agricultural biotechnology if its theoretical foundations – that the DNA genome determines the totality of an organism's inherited characteristics – is demonstrably incomplete [12].

Echoing these points, Philip Regal notes:

“The insertion of a gene may create unforeseen effects in either of two general ways. First, a gene, which apparently integrates randomly at any site or any chromosome, may be inserted at a location that disrupts other cellular function(s). Thus, DNA might be inserted at a site such that it inactivates a resident gene involved in metal detoxification thereby allowing accumulation of the metal....Second, the product of the inserted gene may have unforeseen effects on the plant. Thus, an enzyme introduced to degrade an herbicide may also act on chemically similar substances in the cell to produce toxic by-products” [13].

Some risk analysts assert rather confidently that any protein products from these ancillary genes will be degraded by proteases (enzymes) in animals or by cooking the food sufficiently. Sceptics ask for the animal data and original experiments specific to the GM crops of concern.

They argue, with some plausibility, that the data for the hazard assessment of many of these products are not published in the open literature. Moreover, in the United States, the test protocols are designed by the product's manufacturers.

The US Department of Agriculture (USDA) regulates transgenic crops for their impact on agriculture. However, firms may petition the agency to have the status of their product classified as nonregulated. The US FDA has a voluntary and consultative process for addressing GM crops. Biotechnology companies are asked to refer to a flowchart to decide whether they should consult with the agency about the safety or nutritional quality of their transgenic food products. In the case of the Bt tomato, the US FDA released the data of numerous tests, which some believe ought to be required for every new transgenic food product.

While some view healthy food as food that does not cause or contribute to disease, others use a broader view of health that includes the nutritional quality of the food and its method of production (whether pesticides or herbicides are used). Several countries include in their assessment of GM crops their nutritional composition (amino acids, fatty acids, fibre, phytoestrogens, and lectin). However, without testing standards on nutritional equivalence, there will continue to be debates about how to evaluate the relevant components. Have we used enough animals? Have we fed the animals for a sufficient period of time? Have we used young fast-growing animals in our tests? Have the tests been performed by disinterested and independent scientists? Have the proper biochemistry, immunology, and histology been done on the appropriate organs?

Allergenic effects of GM crops are another area of concern. The Lego model of health risks would raise the caution flag only if the introduced gene codes for a protein that is a known or suspected allergin. Transferring a nut gene into another food product is such an example [14]. There are no assays available to predict definitively the allergenic potential of proteins [15]. Russet Burbank potatoes, which were genetically modified to resist damage by the Colorado potato beetle, were studied for possible allergenic effects. It was the first genetically modified crop with a pesticidal trait that was reviewed by

USDA and USFDA [15]. To evaluate the allergenicity, the agency reviewed data on how many proteins were expressed, the level of the protein expression, whether the proteins have a history of safe use, and whether they share the biochemical profile common to known allergenic proteins. The so-called biochemical profile is a qualitative and inferential means of identifying potential protein allergens, which are present at high concentrations, stable to peptic and tryptic digestion and the acid conditions of the digestive system.

Tests for allergenicity are not part of standard testing. The *New England Journal of Medicine* ran an editorial that addressed the shortcomings of the current policy regarding the transfer or creation of allergens in GM foods [16].

Included among the evolving meanings of health is the concept of health promotion. Consumers who purchase organic foodstuffs consider this choice a part of their personal program of supporting healthy and nutritious food. This was most evident when the USDA received an unprecedented number of complaints in response to its proposal to include GM crops under an organic label. The health considerations of GM crops carry over to pollination of organically grown crops by transgenics. Standards of genetic pollution have not been developed. Under the threat of airborne contamination, some organic farmers may lose their certification because they cannot guarantee that their crops are free of genetically engineered traits. Such losses would erode the confidence of organic consumers in their food supply and in their capacity to fulfill a program of health promotion.

The health models for evaluating GM crops, whether simple or complex, whether mechanistic or organismic, are embedded in international trade and equity issues that are not always transparent. The mainstream media in the United States has tried to explain the difference between European and US responses to GM crops by focusing on the confidence consumers have or lack in their regulatory agencies. According to a recent *New York Times* story: "There is no government agency in Europe of the regulatory rigor of the United States Food and Drug Administration to build consumer confidence..." [17]. Based on this view, the European distrust of their regulatory agencies led to their lack of confidence in the safety of transgenic food. However, this explanation fails to account for the international trade and equity considerations that underlay some of the conflicts. How do we explain the Canadian opposition to BST but its apparent acceptance of transgenic salmon? What do we make of the US polls showing an overriding demand for labelling of GM food and the intense US opposition to carrying such food products under the organic label? How can we understand France's commitment to nuclear technology while opposing agricultural innovations like hormone-fed animals? Why is Europe concerned about the spread of antibiotic resistance in biogenetic crops when over the counter uses of antibiotics are unrestrained? And what are we to make of US consumer opposition to pesticide residues in food (like Alar and EDB) that were declared safe by US regulatory agencies? The controversy over the safety of genetically engineered food products consists of an entangled web of issues involving health, basic science, applied ecology, trade, international equity, the idea of naturalness, the control of genetic resources, and confidence or lack thereof in new technologies [18]. Perhaps this helps to explain the lack of coherence in the political and scientific discourse and the naively reductionist explanations for both genes and the social response to GM food.

### 3 Depolarizing the controversy

Few efforts have succeeded in depolarizing the controversy over the safety of GM crops. During 1999 the gap in mutual understanding between protagonists and antagonists has widened. Moreover, the conflicts have intensified both in Europe and the United States after a long period of US quiescence. If any progress can be made in fostering greater mutual understanding, it will require three elements. First, there should be open discussions in the scientific community about what is known and what is not known about plant genetics. These discussions should focus on the prospect of unanticipated phenotypic changes in plants from novel transgenes: what is the probability of such effects; can they be identified before a product is marketed? Can such effects have health or ecological consequences? We have to know what the scientific literature tells us but also what questions are not resolved in the scientific literature. It is incumbent on the scientific community to close the knowledge gap between the Lego and ecosystem models of the plant genome before it gives its imprimatur to genetically modified food.

Secondly, we must recognize legitimate demands for broadening the assessment of biotechnology products. In *Biotechnics and Society* I identified seven factors for the assessment of new biotechnology products. They are: *ecological impacts* including the product's direct and indirect effects on natural systems, sustainability, and biodiversity; *health effects* on humans; *ethical soundness* or how the product impacts on ethical norms, moral beliefs or general quality of life principles; *economic productivity* including contributions to the efficiency of production, creation of new wealth or jobs and international markets; *distributive justice* such as the contributions of the product to redistributing resources or concentrating wealth; *social needs* – does the product meet an important social need or is the need market driven; *market demand* – whether or not there is a social need, is there a market demand?

While it is generally understood that for-profit companies are not likely to make production choices based on all these variables, nevertheless, there ought to be some public bodies in whose purview it is to explore these factors. A social guidance system for biotechnology that focuses on the most egregious and direct health effects but avoids long-term effects and other social concerns will eventually lose public confidence. Nearly a decade ago comments I made about the state of biotechnology could not be more apt today.

“Too many questions related to the effects of biotechnology are defined outside the responsibility of government. Too many of our agencies of government conceive of their role as promoting innovation and development rather than assessment and selectivity. Too many of those in whom we expect objectivity have vested interests in the financial success of a technology... The inevitable outcome of this situation is that organized efforts by non-governmental groups give up working with federal agencies and work directly with the public” [19].

Finally, consumer sovereignty for new biotechnology products should be honoured. This means that consumers must have a choice. And to have a choice there must be labels on genetically modified food. Whereas consumers who do not wish to be first users of products like artificial fat or sugar substitutes can make that choice, consumers who are presented with new bioengineered products cannot decide to avoid those products since labelling is not currently required and rarely used.

## References

- 1 National Research Council. (1989) *Field Testing Genetically Modified Organisms*, Washington, DC: National Academy Press, p.64.
- 2 Maryanski, J.H. (1995) 'US Food and Drug Administration Policy for foods developed by biotechnology' in *Genetically Modified Foods: Safety Issues*, Engel, K., Takaoka, G.R. and Teranishi, R. (Eds.) Washington, D.C.: American Chemical Society, p.16.
- 3 Millstone, E., Brunner, E. and Mayer, S. (1999) 'Beyond substantial equivalence', *Nature*, Vol. 401, pp.525-6, 7 October.
- 4 Rissler, J. and Mellon, M. (1996) *The Ecological Risks of Engineered Crops*, Cambridge, MA: The MIT Press, p.38.
- 5 Lappé, M. and Bailey, B. (1998) *Against the Grain*, Monroe, ME: Common Courage Press, p.14.
- 6 Ho, M-W. (1998) *Genetic Engineering: Dream or Nightmare*, Bath, UK: Gateway, p. 131.
- 7 Pusztai, A. Interview (1999) <http://wkweb4.cableinet.co.uk/pbrown/index.htm>rgies to transgenic foods – questions of policy. *New England Journal of Medicine*, Vol. 334, pp.726-7, 14 March.
- 8 Kessler, D.A., Taylor, M.R., Maryanski, J.H., Flamm, E.L. and Kahl, L.S. (1992) 'The safety of foods developed by biotechnology', *Science*, Vol. 256, No. 1747-9; 1832, 26 June.
- 9 Rotman, D. (1998) 'The next biotech harvest', *Technology Review* Vol. 101, pp.34-41, Sept/Oct.
- 10 US FDA. (1998) 'Guidance for industry: use of antibiotic resistance marker genes in transgenic plants', *Draft Guidance*. 4 September, <<http://vm.cfsan.fda.gov/~dms/opa-armg.html>>
- 11 Ho, M-W., Ryan, A. and Cummins, J. (1999) 'Cauliflower mosaic viral promoter – a recipe for diasaster?' *Microbial Ecology in Health and Disease* Vol. 11, No. 4, pp.1-8, <<http://www.scop.no/mehd/ho>>.
- 12 Commoner, B. (1999) The Once and Future Threat of the Petrochemical Industry to Environmental Health. *Talk given at the symposium to commemorate the 5th Anniversary of the Environmental Bill of Rights*, Toronto, Ontario, 15 February.
- 13 Regal, P. 'Are genetically engineered foods safe? A scientist's quest for biosafety', <http://biosci.umn.edu/~pregal/foodsafety.htm>
- 14 Nordless, J.A., Taylor, S.L., Townsend, J.A., Thomas, L.A., and Bush R.K. (1996) 'Identification of a brazil-nut allergen in transgenic soybeans', *New England Journal of Medicine*, Vol. 334, pp.688-692.
- 15 Lavrik, P.B., Bartnicki, D.E., Feldman, J., Hammond, B.G., Keck, P.J., Love, S.L., Naylor, M.W., Rogan, G.J., Sims, S.R. and Fuchs, R.L. (1995) 'Safety assessment of potatoes resistant to Colorado potato beetle', in *Genetically Modified Foods: Safety Issues*, Engel, K., Takeoka, G.R. and Teranishi, R., (Eds.) Washington, D.C.: American Chemical Society, pp.148-59.
- 16 Nestle, M. (1996) Allergies to transgenic foods – questions of policy, *New England Journal of Medicine*, Vol. 334, p.726-7,
- 17 Hoge, W. (1999) 'Britons skirmish over genetically modified crops', *New York Times*. 23 August.
- 18 Krimsky, S. and Wrubel, R. (1996) *Agricultural Biotechnology and the Environment*, Urbana, IL: University of Illinois Press, pp.212-231.
- 19 Krimsky, S. (1991) *Biotechnics and Society*, New York: Praeger, p.229.