

# *Who Controls and Who Will Benefit from Plant Genomics?*

By:

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Presented February 19, 2000 Before --

## **“The 2000 Genome Seminar: Genomic Revolution in the Fields: Facing the Needs of the New Millennium”**

AAAS Annual Meeting  
Washington, D.C.

The practical impact of agricultural genomics in the new millennium is difficult to project. The sciences key to biotechnology and genomic technologies are developing quickly. Public and private sector roles and investments are clearly evolving. The capacity to identify and move genes across species barriers has moved ahead far faster than our understanding of gene function and the ways genetic modification may affect function at the molecular, cellular, and especially organismal and ecosystem levels.

The policy arena is unsettled and the marketplace borders on chaotic. On a global basis GMOs have emerged as a universally pressing issue, linking North and South and farmers on all continents in a melting pot of science-trade-economic tensions. Contrary to the wishful thinking of some biotech advocates, public opposition in the United States to foods derived from GMOs is likely to grow as consumers learn more about the technology. The patent and intellectual property arena is a minefield and already is limiting the free exchange of germplasm, ideas, and research tools.

Agricultural biotechnology and plant genomics clearly have great potential to help solve agricultural production and food security challenges. But people are asking, and will continue to ask, whether this promise is being realized. Exactly who stands to benefit and who might end up bearing the costs and unintended consequences as the agricultural biotechnology revolution forges ahead?

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Recent developments are not encouraging and explain in large part why public skepticism is growing. This skepticism may lead to new barriers and costs for those wishing to push the revolution onward. Today I share my sense of how the government and biotech industry are misreading public sentiment and concern. I suggest some practical steps that could help relieve growing tensions and broaden support for both public and private investments in agricultural genomics and biotechnology.

## **A. The Role and Limits of Genetic Modification**

One of the reasons many people worry about agricultural biotechnology is the assumption in some circles that just about any farm production or pest problem can be solved through genetic modification. Put in simplest terms, genes are destiny; get the genes right and any problem will disappear, or at least become much easier to manage. This notion rests on a dangerous lack of understanding of what goes on in an agricultural ecosystem and is one reason why biotechnology makes many people nervous.

Farming entails the management of complex biological systems. Success depends upon managing crop and animal growth close to the limits of natural and biologic resources, given the heat units and moisture Mother Nature is kind enough to provide in a given season. Stress from all sources must be managed so that genetic yield potential is not lost, to the full extent that is economically practical. To reach this goal pests must be managed so that weed competition, insect damage and diseases are kept below economic threshold levels.

Genetic improvement, whether through classical breeding or biotechnology, is no substitute for good judgement in the design of farming systems, nor for attentiveness and skill in day-to-day farm management.<sup>1</sup> In a perfect world, resources available to bring about genetic improvement would be targeted principally toward removing those barriers to yield or crop quality that are inherently genetic or which can only be addressed through genetic modification because of economic considerations (e.g., overcoming rust diseases in small grain). Over most of the last four decades, this has been largely the case but since the early 1990s, there has been a steady shift of breeding emphasis toward compatibility with various pesticide- and toxin-based pest management technologies. For example, Illinois corn growers were offered 23 corn hybrids on the Pioneer website in early 1999. Of these, 10 were Bt-transgenic and three were herbicide tolerant (Benbrook, 1999b, <http://www.biotech-info.net/IWFS.pdf>). Pioneer listed 20 “value-added” attributes across the 23 corn varieties, of which 13 were pest management related (65 percent). Herbicide-tolerant soybean varieties were comparably prominent in Pioneer’s 1999 soybean varietal offerings to Illinois farmers.

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<sup>1</sup> Dr. Ann Clarke of the University of Guelph has warned against over-reliance on genetic modification to solve what are inherently management problems. See papers posted at <http://www.plant.uoguelph.ca/faculty/eclark.htm>.

One of my greatest concerns about agricultural biotechnology is that many companies are over-promising what genetic change can deliver and that farmers may come to believe that genetic improvement can take the place for stewardship and skill in managing farming systems.

Asking too much of *any* genetic, chemical or biological technology is a near-universal recipe for trouble. Biotechnology does not change this reality. Ironically, the benefits delivered by a transgenic crop variety in a given farming system will often be inversely proportional to the scope of change brought about by it.

A contemporary case in point -- farmers are likely to lose a valuable and safe herbicide as a result of over-reliance on Roundup (glyphosate) Ready soybeans and corn.<sup>2</sup> Glyphosate resistance in some weed species has already emerged and shifts in weed communities is undermining efficacy in some parts of the Cornbelt. Still, this technology could prove sustainable and profitable for both farmers and companies if relied on more modestly and managed in ways that avoid resistance and limit selection pressure on weed communities. If farmers lose Roundup as an effective herbicide, it will not be because of an inherent flaw in the molecule or even herbicide tolerant technologies. The failure will be tactical and traced to how the technology is incorporated within farming systems and managed across agricultural landscapes.

## **B. Promising Applications of Genomics and Biotechnology in Food and Fiber Production**

Some applications and aspects of biotechnology and genomics in agriculture are going to continue making people nervous:

- Applications inconsistent with proven principles of sound biologically based agricultural systems, for example herbicide tolerant plants and Bt-transgenics.
- Use of antibiotic marker genes and reliance on powerful viral promoters.
- Moving growth hormones from species to species.
- Technologies driven largely by an opportunity to market a new product in order to capitalize on intellectual property rights.

Studies continue to document already recognized problems with many GMO varieties like pest resistance, erratic performance, poor economic returns to farmers, and non-target and ecological impacts. Ongoing and future work is sure to uncover new and unforeseen problems since nature is never static. Biotechnology does not short-circuit the adaptive capacity of organisms and ecosystems and indeed in some instances likely will shift them into over-drive. Most consequences will be performance-related, but new food safety and health-related risks will emerge as well.

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<sup>2</sup> For information on the emergence of weeds resistant to Roundup, see <http://www.biotech-info.net/herbicide-tolerance.html#soy>. Reasons why Roundup Ready soybeans have been so popular, despite their relatively higher costs are described in [http://www.biotech-info.net/RR\\_yield\\_drag\\_98.pdf](http://www.biotech-info.net/RR_yield_drag_98.pdf).

Over time, scientists will piece together the genetic, physiological or ecological roots of such problems, a necessary step in building confidence in the regulatory process. Policy decisions in the next half-decade will determine whether and how this new information is used in distinguishing between beneficial technologies and those that are not worth the costs and/or risks they impose. Thus far, regulators have faced a manageable number of decisions. The number, scope, complexity and potential significance of applications submitted – and regulatory decisions to make – will grow exponentially in the years ahead. The U.S. government’s policy infrastructure is already shaky, especially the so-called “coordinated framework” put in place in the mid-1980s.

An increasing number of research articles on potential GMO risks are appearing in scientific literature. Those who continue to argue that there is no evidence or reason for caution will not be taken seriously. The same applies to biotech critics who paint with too broad a brush and dismiss all biotechnology as inherently evil. The media, markets, and society will begin to recognize and discount extreme messages. Still, a core challenge will remain - how can society form a reasonably stable consensus to move the science and technology forward, given how divisive these issues have become and how strongly many people feel, pro and con?

Bringing a degree of balance to R+D objectives is one element of forming such a consensus. Right now in the agricultural arena, commercial interests and the conventional pesticide paradigm are clearly driving the technology. To date government has shown little will or capacity to foster a greater diversity in research approaches and paradigms.

Some influential players and companies seem to appreciate that the time has come to begin hedging the enormous bet and investments already made on agriculture biotechnology. Others would “rather fight than switch.” Eventually dialogue must replace confrontation. As this occurs, one useful exercise will be for promoters and skeptics to mutually identify applications of genomics and biotechnology in food production and processing that seem worthy of public and private investments despite whatever risks they may entail. Herein I discuss some candidates.

### **Promising Biopesticide and Pest Management Applications**

Agriculture clearly needs new and safer tools to manage a range of insects and plant diseases. Farmers and pest management specialists must also recognize that narrow, specific solutions – whether cultural, chemical, or genetic – are universally vulnerable when relied upon unilaterally across much of an agricultural landscape.

Progress is being made in the development and adoption of biointensive Integrated Pest Management systems (BioIPM), yet managing grower risk of major losses remains a major constraint. Fortunately, the pesticide industry has discovered and brought to market some very effective, much safer and selective biopesticides and closely



resistance development will be essential in devising effective resistance management strategies. Genomics will make it possible to unravel the genetic basis of resistance, perhaps soon enough to design and implement effective management strategies.

A potential role for jasmonic acid in triggering plant defenses is described in a fascinating 1999 paper in *Nature* (Thaler, 1999; <http://www.biotech-info.net/jasmonate.pdf>). Most biopesticides work through some direct impact on the development, feeding behavior, energy metabolism or reproduction of the target pest. There are other, more elaborate mechanisms, however, such as triggering plants to emit chemicals that attract insect predators and parasitoids. Thaler was able to accomplish this goal in California tomato fields. Applications of jasmonic acid triggered a response in the octadecanoid pathway, which appears to produce volatile chemicals that serve as a signal to certain insect predators. In this experiment caterpillar predators were attracted to treated plants and reduced feeding damage significantly.

Several teams are also looking for ways to trigger or reinforce systemic acquired resistance (SAR), a widely studied mechanism through which a plant attains the ability to overcome pathogen infection and other pest threats. There is already one chemical pesticide on the market designed to help trigger SAR (the Novartis product Actiguard, which contains the active ingredient acibenzolar-S-methyl). Oldroyd and Staskawicz have shown that transgene-induced SAR can broaden the spectrum of disease control possible through stimulation of SAR (Oldroyd and Staskawicz, 1998; [http://www.biotech-info.net/GE\\_tomato.html](http://www.biotech-info.net/GE_tomato.html)). Many companies are working on combined approaches that entail genetic modification to enhance SAR within a cultivar in conjunction with promoter genes linked in some way to the application of a chemical trigger, like jasmonic acid or the Novartis product Actiguard.

While plant pathologists are focusing on ways to trigger or augment SAR, entomologists are pursuing a number of other strategies that reinforce or broaden the efficacy of biological control approaches. A Japanese team increased the susceptibility of armyworms to baculovirus by engineering rice plants to express an entomopoxvirus gene encoding for a virus enhancing factor (EF) (Hukuhara et al., 1999; <http://www.biotech-info.net/baculovirus.html>). The experiment was remarkably successful - the dose of baculovirus needed to infect 50 percent of armyworm larvae feeding on transgenic rice leaves was reduced 260-360 times compared to non-engineered plants.

In general, it seems likely that genetic modifications that strive to amplify or otherwise reinforce the effectiveness of a natural plant defense mechanism are likely to prove more stable and less prone to pleiotropic impacts than transformations creating wholly new mechanisms. They should also be more acceptable to the public.

## **Dealing With New Pests**

New pests and strains of disease organisms emerge annually in new environments. Some people believe more virulent pathogens, exotic species and hard-to-control insects are emerging as problems faster than ever before (Ho et al., 1998 2000). Some people hypothesize that biotechnology, intensive farming and global trade may be contributing to the increased pace of natural adaptation and the dispersal of pest species.

Geminiviruses are an important contemporary example. Another symposium speaker, Dr. Roger Beachy, has worked on a team demonstrating the capacity of geminiviruses to exchange DNA; a recent *Science* article reported that over 1,000 (naturally) recombinant strains have been found, including some from species with very different DNA sequences (Moffat, 1999; <http://www.biotech-info.net/geminivirus.html>). As the organism expands its host range and becomes more virulent, more and more farmers face losses. The article goes on to explain that the search is on for resistant cultivars and that classical and/or genetic engineering techniques may be used to create them. The reader is left with the impression that only genetic modification can solve the problem posed by geminiviruses, despite the fact that the organism has proven itself very capable of evolving around once-effective genetic solutions.

Classical or engineered resistance is only one tactic available for use against geminiviruses. These viruses help from insects to reach crop fields, spread within them, and induce infection. For years farmers in Florida have controlled these and related viruses most successfully through a multi-tactic system that rests upon aggressive elimination of sources of inoculum and timely control of their insect vectors. Even if plant breeders develop new sources of resistance that can be moved into commercial cultivars, resistance will last only if combined with other tactics that will lessen the chance of infection and delay the emergence of new strains. Deployment of such tactics must remain at the core of farmer-driven resistance management, regardless of whether the cultivar comes from classical or transgenic breeding techniques.

The tools of biotechnology have much to offer in the discovery of new tactics and their integration into BioIPM systems, yet these options continue to attract very modest levels of public and private sector R+D resources. This leaves our national effort to better manage pests like geminiviruses unbalanced and unnecessarily vulnerable. It also suggests that something other than the goal of finding affordable and stable solutions is driving the technology development process.

## **Understanding the Ecological Impacts of Genetic Engineering**

By 1996 there were over 25 million acres in the U.S. planted in transgenic plant varieties (for details, see <http://www.econ.ag.gov/whatsnew/issues/biotech/Table1.pdf>). About this time limited independent research began in a few U.S. laboratories on possible ecological impacts. The scope of work supported by U.S. Department of Agriculture funding remains limited; the USDA has allocated less than \$2 million annually in support

of the development of ag-biotech risk assessment methods, clearly a modest sum compared to the billion-plus investment annually in agricultural biotechnology.

The results of the first wave of GE-ecological studies in the United States (those carried out since 1996) are now appearing in scientific journals.<sup>3</sup> Most rely heavily on genomic and biotechnology techniques. Many focus on the persistence of GMOs in various environments and their ability to exchange DNA with other organisms. These are among critical variables determining the likelihood and extent of horizontal gene transfer.

According to Tappeser and colleagues at the Institute for Applied Ecology in Germany, “Horizontal gene transfer is now recognized to be the main avenue of exchange of genetic material in the microbial world, and hence also of the exchange and spread of antibiotic resistance genes” (Tappeser et al., 1998; [http://www.biotech-info.net/GMO\\_update.html](http://www.biotech-info.net/GMO_update.html)). Recent work has shown that the digestive systems of invertebrates and vertebrates - from worms to mice to man - is a likely place where such transfers can occur. The excellent 1998 review article by Tappeser et al. cites several studies documenting such transfers. In addition, it is also becoming clear that gene flows can occur in just a matter of minutes, even seconds (Brockmann et al., 1996) and that there are often multiple mechanisms that might come into play under variable conditions.

Biolog GN metabolic fingerprinting was used by a team to assess the differences in the microbial communities colonizing otherwise similar conventional and transgenic alfalfa varieties. The results “suggest that transgenic plant genotype may affect rhizosphere microorganisms and that the methodology in this study may prove a useful approach for the comparison of bacterial communities” (Di Giovanni et al., 1999; [http://www.biotech-info.net/transgenic\\_alfalfa.html](http://www.biotech-info.net/transgenic_alfalfa.html)). These techniques may prove useful for the analysis of the impacts of Bt-corn hybrids for rootworm control.

### **Microbial Biocontrol of Soil Pathogens**

Microbial biocontrol of damaging soil microorganisms (hereafter called rhizobacteria) represents a vast and largely untapped frontier (Cook, Bruckart et al., 1996; [http://www.biotech-info.net/safety\\_microorganisms.html](http://www.biotech-info.net/safety_microorganisms.html)). It is too expensive for farmers to use fumigants and other toxicants to control soil pathogens in most major grain, row and field crops. Very few farmers in developing countries can afford such costly methods to deal with soil-borne pests. For this reason cultural practices, particularly crop rotations, have been crucial worldwide in managing common root pathogens. Success tends to occur when a combination of practices creates a soil environment sufficiently conducive to non-damaging or beneficial microorganisms, such that they collectively keep Pythium, Rhizoctonia, or take-all diseases from decimating root systems.

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<sup>3</sup> Fortunately, early in the 1990s several European research institutes had initiated serious research on the ecological impacts of transgenic crops. For this reason, most of the cutting edge science on agricultural biotechnology and possible ecological impacts comes from overseas.

In the Pacific Northwest, Dr. James Cook and colleagues have worked on microbial biocontrol of these common wheat root diseases for some 30 years (for an excellent overview, see Cook et al., 1995; <http://www.biotech-info.net/rhizobacteria.pdf>). As the tools of biotechnology came along, progress accelerated. Still, many steps were necessary to progress from recognizing a potential microbial biocontrol mechanism to developing a means to take advantage of it. In August 1988, two members of the team published a paper showing the role of the antibiotic phenazine-1-carboxylate in suppressing take-all decline and other root pathogens (Thomashow and Weller, 1988; <http://www.biotech-info.net/biocontrol.html>). Genomic and GE techniques that would be regarded as primitive today were used to create mutant strains of bacteria expressing the genes producing the phenazine antibiotic. The importance of the natural *Pseudomonas fluorescens* strain 2-79 in the production of this antibiotic was documented in a 1990 paper (Thomashow et al., 1990; [http://www.biotech-info.net/phenazine\\_production.html](http://www.biotech-info.net/phenazine_production.html)).

An August 1992 paper (Mazzola et al., 1992; [http://www.biotech-info.net/phenazine\\_biosynthesis](http://www.biotech-info.net/phenazine_biosynthesis)) showed that the antibiotics emitted by naturally occurring rhizobacteria were critical to their ability to survive in Pacific Northwest wheat field soils and that furthermore, these bacteria can play a critical role in the suppression of root diseases. Next the team characterized a 6.5 kb fragment from *Pseudomonas fluorescens*, strain Q2-87, the region that accounts for the production of another phenazine (Phl) antibiotic of interest. This key work showed that the 6.5 kb fragment contained the Phl biosynthetic locus and that insertions into this fragment affected Phl production in a variety of ways.

Cooperative work with Swiss scientists further refined understanding of the gene fragment with the Phl locus and drew upon it to produce a probe to test soils for the presence of strains of bacteria producing Phl. Two phenotypically distinct groups were found in soils from the U.S., Europe and Africa (Keel et al., 1996; <http://www.biotech-info.net/fluorescent.html>), leading to the insight that the genes for production of Phl are highly conserved in nature. In 1997 the team published a method to quantify the production of Phl in vitro and in the rhizosphere.

This methodology would make it possible for the team to screen a large number of indigenous strains of bacteria, seeking those with the characteristics needed to produce a competitive and effective microbial soil inoculant or biopesticide. Late in 1997, the team informed the USDA and EPA of its intent to carry out a small field scale test of a transgenic microbial pesticide. The microbial pesticide was formed by cloning the Phl biosynthetic pathway from *Pseudomonas fluorescens* strain 2-79 into *Pseudomonas fluorescens* strain Q8R1-96, which was known to be a better root colonizer. On December 19, 1997 the EPA published a notice in the Federal Register announcing receipt of the notification and inviting public comments (Knox, CFR pages 66624-66625; see [http://www.biotech-info.net/receipt\\_notification.html](http://www.biotech-info.net/receipt_notification.html)).

This application of biotechnology was the first supported by Consumers Union in official comments submitted to the EPA. The comments were submitted in January 1998 ([http://www.biotech-info.net/pseud\\_comments2.html](http://www.biotech-info.net/pseud_comments2.html)). The only critical comment and suggestion involved the need to replace the antibiotic marker gene used in the original transformation. Consumers Union supported this application because it was -

- Largely compatible with proven Integrated Pest Management principles;
- Involved the exchange of genes between closely related microorganisms (indeed Dr. Cook and colleagues hypothesize that the same exchange of genetic material had likely occurred in the past through natural bacteria conjugation); and
- There was no evidence that the new strain would gain a major competitive advantage or create any secondary problems.

### **Other Applications Targeting the Rhizosphere**

Work is also underway in an effort to develop transgenic plants for phytoremediation and molecular farming (Gleba et al., 1999; <http://www.biotech-info.net/roots.pdf>). The idea is to “take advantage of the ability of plant roots to absorb or secrete various substances.” In a compelling article in the *Proceedings of the National Academy of Sciences*, Gleba and colleagues point out that up to 10 percent of the photosynthetically fixed carbon is secreted through roots and state that -

“Intuition and limited published data suggest that root-secreted compounds have a wide spectrum of biological activities including protection against biotic and abiotic stresses...The unexplored chemical diversity of root exudates is an obvious place to search for novel biologically active compounds.”

An August 1999 article in *Science* reviewed efforts to develop more salt tolerant crops through genetic engineering, an idea first proposed 20 years ago (Frommer et al., 1999); <http://www.biotech-info.net/salt.pdf>). A team led by Apse identified and overexpressed the Na<sup>+</sup>/H<sup>+</sup> antiport gene in *Arabidopsis*, creating significantly more salt-tolerant plants (Apse et al., 1999; [http://www.biotech-info.net/salt\\_tolerance.html](http://www.biotech-info.net/salt_tolerance.html)). Other strategies will no doubt emerge to try to increase the production potential of high saline soils. The economics of such technologies will eventually have to be evaluated relative to a variety of proven methods to either reduce salt levels in soil or limit further deposition.

Since soil salinity is highly correlated with irrigation water quality and management and cropping system design, it is likely that the most cost-effective and sustainable solutions will involve a heavy dose of prevention, in addition to perhaps some increases in crop salt tolerance. If scientists and breeders try to push salt tolerance too far they are likely to trigger pleiotropic effects that impose additional costs and complications on farmers. It is also worth noting the complex linkages across social

goals in regions dealing with high saline soils. In most cases, such areas are arid and high quality drinking water is a valuable public good in limited supply. Reducing the salt content in freshwater resources is often a goal of water quality programs designed to improve human health and preserve fisheries and biodiversity. Sometimes high saline conditions are simply caused by grossly inefficient and excessive fertilization, a problem whose solution almost always pays for itself.

### **Impacts on Soil Quality**

Soil quality is generally defined as the capacity of a soil to take in, store and purify water, to hold and recycle nutrients, to support a diverse and robust biotic community, and to suppress pathogens and other pests. A seminal 1998 study in *Nature* by van der Heijden and colleagues showed that the diversity of mycorrhizal fungi plays a key role in determining the productivity of soil ecosystems (van der Heijden et al., 1999; <http://www.biotech-info.net/mycorrhizal.html>). An overview by Read in the same issue speculates that greater fungal biodiversity expands the range of mechanisms through which microbial interactions can help plants deal with various sources of stress and competition (Read, 1999); [http://www.biotech-info.net/plants\\_web.pdf](http://www.biotech-info.net/plants_web.pdf)). A team in Denmark has shown that indigenous soil bacteria can serve as a sink for plasmid-borne antibiotic resistance traits from *E. coli* added to agricultural soils (Sorensen et al., 1999).

Holmes and colleagues in Oregon studied the impacts on soil biota of the addition of genetically engineered bacteria used in ethanol production (Holmes et al., 1999). They conducted a microcosm study in sandy soil supporting wheat plants. An engineered strain of the bacteria *Klebsiella planticola* stimulated the numbers of bacterial and fungal feeding nematodes and resulted in wheat plant decline and death, whereas plants survived following addition of the non-engineered strain. Their experiment showed the importance of plant-bacteria-nematode interactions in determining the impacts of changes in soil microbial communities and that impacts need to be assessed across several trophic groups of organisms.

Disease suppressive soils arise because of interaction between plants and soil organisms. Key work by Goodman, Handelsman and colleagues at the University of Wisconsin have documented phenotypes in several plants that seem better able to trigger the disease suppressive potential of certain soil microorganisms, particularly *Bacillus cereus* strains (Smith et al., 1999; [http://www.biotech-info.net/genetic\\_basis.html](http://www.biotech-info.net/genetic_basis.html)). Their work shows that it is not just the soil, nor plant genetics that give rise to disease suppression, but an elaborate series of communications that arise from organisms in the soil to the growing plant and back to soil organisms through root exudates.

It is also clear that a range of climatic, nutrient, cropping, and soil structure issues play key roles in modulating the communication between soil organisms and plants. One implication is clear - breeders will be able to create cultivars more resistant to a given disease by moving into a commercial variety specific genes that amplify a given plant defense response. But field performance may prove spotty because there are

typically many different soil pathogens competing for a chance to thrive, as well as a variety of conditions that can break down channels of communication between soil organisms and plants. For this reason, the cost of dealing with root diseases through specific plant genetic modification may prove to be prohibitive. Instead, the best strategies may be those that diversify or reinforce below-ground microbial biocontrol mechanisms or those that generically strengthen plant defense systems.

The first transgenic variety designed to exude a toxin through its root system - a Bt-corn developed by Monsanto -- is scheduled to reach the U.S. market in crop year 2001 or 2002, pending regulatory approvals. Impacts of this technology on soil food-webs and plant health and productivity are the major new concerns raised by this Bt-corn, engineered to control corn rootworm during its larval stage in the soil.<sup>a</sup>

The soil quality and plant health consequences of transgenic plants will trigger extensive debate because of growing interest in the role of indigenous soil organisms in sustaining productive and profitable farming systems. Some people argue that it is not now possible to evaluate the soil quality impacts of transgenic cultivars because there is no baseline of knowledge from which to monitor potential adverse impacts. Indeed, some of the basic ways plants communicate through their root systems with soil microorganisms are just now being identified. Because of our lack of baseline knowledge, some experts argue against the widespread planting of such varieties. Others respond by stating that tillage, crop rotations, and pesticides, especially soil fumigants have been profoundly altering soil microbial communities since farming began, and that ignorance of soil quality impacts never previously stopped the technology adoption process.

This debate frames a host of critical science and policy questions. Consensus and solid answers will take years to crystallize because so little is known about soil microbial ecology and how farming systems impact soil health, in turn influencing plant health and productivity. In the world of policy and research priorities, we have still not come to grips with serious impacts, and in many cases, degradation of soil microbial communities over the last six decades. Thus many ask "Why hold biotechnology to a higher standard?" One reason would be a priori evidence that transgenic technologies might impact soil microbial communities in ways that are qualitatively different or irreversible relative to other technologies and farming practices, like tillage, fertilization, or irrigation.

Genomics and related biotechnology research could produce critical information to determine whether a threshold level of qualitatively distinct impacts has been met. To do so new research must focus on -

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<sup>a</sup> For information on this new technology, see "Ag BioTech InfoNet" at <http://www.biotech-info.net/rootworm.html>. An overview of soil quality concerns is presented at [http://www.biotech-info.net/microbial\\_communities2.html](http://www.biotech-info.net/microbial_communities2.html). Detailed comments were submitted January 7, 2000 to EPA on Monsanto's application for an Experimental Use Permit (EUP) on this technology, accessible at [http://www.biotech-info.net/Corn\\_EUP.pdf](http://www.biotech-info.net/Corn_EUP.pdf).

- Characterizing the short-term and longer-run fluctuations in soil microbial and invertebrate communities as a result of root exudates and toxins in root tissue. This area of work needs to ultimately trace impacts on soil and terrestrial food-webs.
- Linking these fluctuations and food-web changes to nutrient cycling and bioavailability (especially of phosphorous), changes in pest complexes and pressure, the triggering of plant immune response, and impacts on non-target organisms.
- Monitoring the emergence of resistance in soil organisms, including non-target species, in order to detect unexpected shifts in species fitness and competition.

### **C. Reconciling Emerging Science with Regulatory Policy**

Biotech proponents argue that genetic engineering differs little from conventional breeding and that it is more precise and poses no new or hidden risks. It is increasingly hard to reconcile these simplistic assertions with emerging scientific knowledge. Of course, some applications of biotechnology are very similar to classical breeding or bring about a combination of genetic traits that may have actually occurred in nature. But much of the work underway entails moving genes across species barriers.

When the tools of biotechnology are used to move novel genes into an organism, that organism will always respond and adapt in a variety of ways. Short-term responses will largely affect whether the genetic alteration is stable and useful relative to the desired change and whether the transformation leads to the silencing or changes in the expression of other desirable genes. Longer-term impacts and cellular responses can lead to gene silencing, codon bias, functional instability, and a range of pleiotropic effects.

Many of these adaptations will be benign or of no consequence in most and perhaps even all circumstances. But under conditions of drought stress, when a particular nutrient is over- or under-supplied, when it is hotter or cooler than normal, when certain pests attack plants, in the presence of certain bacteria, and especially, when there are combinations of the above, plant physiological and immune systems will be forced into a sort of hyper-drive. It is under such conditions that unexpected and possibly risky consequences of genetic transformation are most likely, leading to what might be called “stress induced pleiotropic impacts.”

Examples of stress induced pleiotropic effects have already been documented. Petunias engineered to produce salmon red flowers broke down under conditions of stress, producing progressively fewer salmon red flowers (Meyer et al., 1992). Roundup Ready cotton boll drop appears linked to weather-induced stress (Fox, 1997, [http://www.biotech-info.html/cotton\\_drops\\_bolls.html](http://www.biotech-info.html/cotton_drops_bolls.html)), as is uneven expression of

Bt toxins in cotton plants. Heat-induced yield problems with Roundup ready soybeans also appear to be a stress induced pleiotropic effect (Coghlan, 1999).

### **Regulating GMO Foods - First Steps**

In the mid-1980s, the United States government adopted the “substantial equivalence” policy based on the notion that foods derived from GMOs should be regulated in terms of their characteristics, and any quantifiable differences from non-GMO foods, rather than according to how they were produced. For the last decade the FDA, USDA, and EPA have received and approved thousands of applications to field test GMOs. Few, if any, applications have been turned down because of concern over risk.

Through their provocative 1999 commentary in *Nature*, Millstone and colleagues triggered a useful debate over the scientific basis and impacts of the “substantial equivalence” policy. This policy lies at the heart of U.S. and European regulatory review and approval processes (Millstone et al., 1999; see [www.biotech-info.net/policy.html#discussion](http://www.biotech-info.net/policy.html#discussion) for the original article, several letters, and further discussion). It is important to assess further the soundness of the substantial equivalence policy, an issue which arose prominently in the public hearings the FDA sponsored in the summer and fall of 1999. A key step in doing so is to determine, since the policy was put in place, whether science has produced new information and insights that suggests or demonstrates gaps in current regulatory testing and reviews.

One way to do so is to review the GMO risk concerns taken into account by regulatory scientists and agencies in the U.S. in the mid- to late 1980s, when the policy was codified, in contrast to risk concerns addressed recently in the scientific literature. A comprehensive review would be a major undertaking; here, I focus just on recent scientific literature that sheds light on a subset of potential GMO risks.

### **Contemporary GMO Food Concerns**

Several recent overview articles and overviews have summarized the major mechanisms through which a GMO crop or food might lead to unanticipated adverse effects, either in the environment or in humans. These include:

- “Long-term effect of GM crops serves up food for thought.” (Butler D., and T. Reichardt, 1999; [http://www.biotech-info.html/long\\_term\\_effect.html](http://www.biotech-info.html/long_term_effect.html))
- “Too early may be too late: Some ecological risks associated with release or escape of recombinant or genetically altered nucleic acids.” (Traavik, T., 1998)
- “Gene technology and gene ecology of infectious diseases.” (Ho, M.W. et al., 1998)
- “Survival, persistence, transfer- an update on current knowledge on GMOs and the fate of their recombinant DNA.” (Tappeser et al., 1998; [http://www.biotech-info.net/GMO\\_update.doc](http://www.biotech-info.net/GMO_update.doc))

- “Genetic engineering is not an extension of conventional plant breeding: How genetic engineering differs from conventional breeding, hybridization, wide crosses and horizontal gene transfer.” (Hansen, M. ,2000; [http://www.biotech-info.net/wide\\_crosses.html](http://www.biotech-info.net/wide_crosses.html))
- “Ten Reasons why farmers should think twice before growing GE crops.” (Clark, A., 1999; <http://www.plant.uoguelph.ca/faculty/eclark/10reasons.htm>)

<b>Table 1: Historical Trends in GMO Publication Citations</b>						
<b>Category</b>	<b>Earliest Citation</b>	<b>Number of Citations</b>				<b>Pre-1990 to 2000</b>
		<b>Pre-1990</b>	<b>1990-1993</b>	<b>1994-1997</b>	<b>1998-2000**</b>	
Search Keywords*						
<b>Gene Silencing</b>						
Gene silencing	1980	1	10	35	63	109
<b>Gene Flow and Transfer</b>						
Codon bias	1992	0	1	3	3	7
CaMV and gene	1989	1	11	10	2	24
Viral recombination	1993	0	1	3	0	4
Foreign DNA	1984	10	16	10	14	50
Naked DNA	1979	13	17	19	22	71
<b>Pleiotropic Effects</b>						
Pleiotropic and transgenic	1989	2	1	4	5	12
*Searches were executed on HighWire Journals search engine at < <a href="http://www.sciencemag.org/searchall">http://www.sciencemag.org/searchall</a> >. Journals in the following categories were selected: Biochemistry, Cell and Molecular Biology; Microbiology and Virology; Plant Sciences; Other Life Sciences; and Medical Research.						
**Searches were conducted in February 2000.						

The major concerns covered in Table 1 are not exhaustive. Several ecological risks are also of recent vintage and belong in a more complete analysis. The earliest identified citations and trends in citation over time are shown. All searches were done using High Wire on the *Science Online* website. Keywords used in the search are shown in the table. For the seven categories in Table 1, the data show that:

- Less than 10 percent of the total number of citations covering seven major areas of risk appeared before 1990. About seventy percent have appeared since 1994. Accordingly, the “substantial equivalence” policy was formed well before many of today’s most important risk concerns had been studied to any significant degree.
- Ninety percent of the total citations on “gene silencing” have appeared in the literature since 1994 and almost 60 percent in just the last two years. Clearly gene silencing qualifies as a ubiquitous phenomenon, and one which is attracting a lot of attention.

- Relatively few studies have explored some critical concerns, e.g. pleiotropic effects.<sup>4</sup>
- The number of papers in some areas like codon bias and naked DNA is accelerating. If current trends continue knowledge in these areas should rapidly expand.

## **D. Control Issues and Implications**

Public attitudes toward GMO foods are shaped by several factors. Some people worry about health risks to themselves, their families, or the public at large. Others worry about ecological impacts. Ethical and religious concerns lie behind the concerns of others. And last, many people are most worried about a set of economic and control issues - patents, intellectual property rights, globalization, questions about who is driving the R+D agenda, distribution of costs and benefits, and impacts on corporate structure and control.

There seems little chance that science is going to alleviate most of the health and environmental risk concerns, at least not any time soon. Given that agriculture is inherently a disruptive and biologically dynamic process, there are bound to be applications of genetic engineering in the food and fiber sectors that lead to problems. Even when isolated and contained, such episodes will reinforce the notion that we do not know enough to predict or manage the consequences following widespread planting of a given transgenic crop or the raising of a transgenic animal.

Likewise, there is no end in sight to worries over patents, intellectual property issues, and corporate consolidation. The reason is obvious - people cringe at the thought that corporations might someday control their genetic destiny, or that of their children. They worry that companies will use this power to extract larger profits from medical treatments. As a handful of companies gain control over crop germplasm, similar concerns arise over corporate control over the food supply. In both cases there are already real-world circumstances and episodes reinforcing these concerns. There are bound to be many more in the next few years given the pressure on biotechnology companies to justify high stock market valuations and attract new investors. Even in the absence of new evidence of health and ecological risks, control issues will keep biotechnology in the news and in the public eye.

### **Cashing in on Patents and Genomics Information**

The rush in the private sector to control gene technology makes people nervous. Last month the popular press in Great Britain covered a story that must have reinforced concerns over the patenting of human genes. The story involves an attempt by the U.S.-based biotechnology company Myriad Genetics to compel British doctors to use their more sensitive breast cancer screening technology. The Myriad Genetics system is based

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<sup>4</sup> Our search did not pick up papers on some pleiotropic effects such as triggering a biologically significant level of expression of allergenic proteins.

on the BRCA1 and BRCA2 genes, over which Myriad holds a patent. British health officials dispute the breadth of the patent and are concerned that the substantially higher cost of the Myriad screen will limit the number of woman who can afford the procedure (“U.S. Firm may Double Cost of U.K. Cancer Checks,” James Meek, *The Guardian*, January 17, 2000).

Without doubt, genomics will lead to many novel and more sensitive diagnostic and screening tools. Their applications and costs, however, will raise all sorts of practical and ethical questions and controversies. If the general public comes to believe that cashing in on intellectual property is inordinately driving how the technologies are used, or that the technologies are widening the gap between rich and poor, the public will force the system to change, one way or another.

In the agricultural arena, companies are now pursuing patents that cover routine physiological pathways and plant defense system responses. Novartis has applied for two patents in Europe (WO 99/35910 and WO 99/35913) covering an observed beneficial yield response when Bt-transgenic corn is sprayed with a number of pesticides, including nicotinoids like imidacloprid and thiomethoxam, the neural feeding inhibitor pymetrozine, a carbamate insecticide, and various herbicides. The claims in the patent cover unanticipated synergistic interactions between applications of various pesticides and yields of Bt-corn and even herbicide tolerant plants. The implications of the information put forth in these patent applications are that -

- GMO crops may be more vulnerable to certain pests than non-GMO varieties;
- Transgenic varieties will, in some circumstances need additional pesticide treatments to achieve maximum yields, perhaps because of some pleiotropic effect on natural plant defense mechanisms in addition to impacts on non-target beneficial insects and microorganisms; and
- In the long run GMO varieties may become more reliant on a broader range of pesticides in order to deal with always-changing pest complexes.

It is conceivable that a company might gain a patent on a gene or set of genes that plays a key role in triggering or modulating systemic acquired resistance (SAR), the production of semiochemicals or antibiotics, senescence, or even something as basic as photosynthesis. The significance of such patents could be enormous, since companies might be able to extract royalty payments from all other companies and public sector laboratories working at the genetic level on the same pathway or immune system response. At a minimum, the constant consideration of intellectual property right issues will continue to impose costs on the system and slow down scientific progress and the exchange of germplasm and breeding and biotechnology tools.

According to a 1999 survey of public sector plant breeders conducted by Steven Price of the University of Wisconsin (Price, 1999; [http://www.biotech-info.net/public\\_private.html](http://www.biotech-info.net/public_private.html)), almost half the breeders reported they had experienced difficulty in obtaining genetic stocks from private companies; 45 percent said that new

restrictions on the exchange of germplasm had interfered with their research; and, about one-quarter reported that such restrictions had gotten in the way of graduate training. According to Price, the need to negotiate “material transfer agreements” (MTAs) is commonly the problem:

“Negotiating these [MTAs] will continue to be difficult until the public and private sectors agrees on a common culture...If every MTA starts with each side putting its most onerous terms forward, then the negotiations will continue to be slow...public sector breeders will be hurt in the near term...in the long run, companies will be hurt by a decrease in trained plant breeders...the public may be hurt by decreased genetic diversity resulting in fewer varietal choices.”

Material Transfer Agreements are a problem in other fields. The Pasteur Institute considers mouse MTAs as “a big administrative burden,” a view clearly shared by many other institutions and scientists. An effort is underway by the International Mammalian Genome Society to develop a simple, standardized mouse MTA that will lower costs and encourage free exchange of mouse research tools (Abbott, 2000; [http://www.biotech-info.net/mouse\\_geneticists.html](http://www.biotech-info.net/mouse_geneticists.html)). Progress dealing with the problem has been made in the United States -- Dupont and the NIH have reached a mutually acceptable agreement over access to Dupont’s patented *Cre-lox* technology that allows certain genes to be removed from specific cells. Problems over access to this technology persist in Europe and within the private sector.

The race by Celera Genomics and Incyte to profit from human genome sequence data is widely covered in both the scientific and lay media (for example, see Butler and Smaglik, 2000, [http://www.biotech-info.net/celera\\_genome.html](http://www.biotech-info.net/celera_genome.html); and Langreth, 2000). The companies are pursuing different strategies: Celera wants to sell access to its proprietary genomics data in return for fees and future royalties; Incyte is relying on patents over key gene sequences to position itself in the path of technology development. Ultimately the success of such companies and approaches will depend on whether the public believes that the rewards they seek and win from the marketplace are commensurate with their contributions in advancing science and technology. It is hard to imagine people accepting a system of patents and intellectual property protection that allows selected companies to extract large profits from genomic discoveries made possible by public and private sector investment over many years.

### **Control of Research Agendas**

The notion that most agricultural production and nutrition problems can be solved by moving a few genes around has clearly been very seductive. It has led Wall Street to invest billions in biotechnology and underwritten the largely hostile takeover of the seed industry by the pesticide industry. It has fundamentally changed the focus and conduct of science in land grant universities, where molecular biology and the pursuit of genetic solutions now dominate departments that used to carry out a wider range of research, including significant applied field and systems-based research.

This enormous shift in resources and the focus of agricultural science has occurred so quickly that there has not been adequate time for much reflection on the sustainability or value of the resulting technologies. The loss of the benefits of research that has been abandoned in favor of molecular approaches has similarly been unexamined. In most quarters enthusiasm over the possible benefits of agricultural biotechnology has been infectious and unbounded. It has led many people to accept on faith that the technologies would generate enough “value added” returns to justify - and pay for - the costs of bringing the technologies to market.

Science and experience are catching up with the myths generated by blind faith in agricultural biotechnology. The true value of biotechnology lies in its ability to provide farmers and those working with them the insights and tools needed to become better managers of the biological processes on which food production depends. Genetic improvements will surely remain a critical part of farming system innovation but over-reliance will lead to problems. The ecosystem and evolutionary forces behind resistance, weed shifts, the interplay of pests and beneficials, soil quality and plant health, and the emergence of new strains of disease organisms are complex, powerful and ubiquitous.

Commercial biotechnology must come to terms with these forces. Much of the value of biotechnology will flow from its ability to help farmers understand and shape these forces rather than its ability to render them moot. Many changes will be required for this paradigm shift to take hold, including a rather significant change in public and private research priorities.

### **Private Sector Priorities**

Private companies have invested most heavily in Bt-transgenic and herbicide tolerant varieties - so-called input traits. These applications of biotechnology have dominated private investment because they were technically possible and offered a new way for companies to extract greater profits from intellectual property rights - both those covering pesticide active ingredients and genes and genetic engineering techniques.

The market success of Roundup Ready (RR) soybeans has been unprecedented in several ways. RR soybean varieties gained market share faster than any other new trait ever introduced. The technology triggered a price war among herbicide manufacturers that has brought down herbicide prices to soybean farmers by about one-third across the board. RR soybeans have earned Monsanto hundreds of millions in “technology fees” linked to the purchase of seed - a new way to profit from intellectual property and seed industry assets. Most of the pesticide-seed industry is now investing heavily in bringing new herbicide tolerant varieties to market, hoping to capture a little of the magic that Monsanto has enjoyed with RR soybeans.

Yet the success of RR soybeans is already leading to trouble. Resistance and shifts in weed communities are occurring that require farmers to make multiple

applications of Roundup in fields where just one application worked for a year or two. Many farmers planting RR soybeans this year will apply two applications of Roundup along with at least one and often two other herbicides. Since RR soybean systems rest almost exclusively on herbicides for weed management, both reliance and average use will increase, contrary to claims that farmers planting these varieties use less herbicides (for more detailed discussion, see Benbrook, 1999a; [http://www.biotech-info.net/RR\\_yield\\_drag\\_98.pdf](http://www.biotech-info.net/RR_yield_drag_98.pdf)).

Experience with Bt-transgenic corn engineered to combat the European corn borer has been similar although not quite as dramatic. The technology has been adopted quickly and generated major income for Monsanto, Novartis, and AgrEvo. Notwithstanding consumer and trade jitters, the future of Bt-corn is suspect because of a range of inter-related ecological and biological problems that are coming into focus - resistance, impacts on non-target organisms and soil microbial communities and food webs, and value to farmers. Purdue University is the latest land grant university issuing a blunt report to corn growers on the economics of Bt-corn (Hyde et al., 2000; [http://www.biotech-info.net/btcorn\\_adoption.html](http://www.biotech-info.net/btcorn_adoption.html)). Because corn borer infestations are episodic, the extra cost of Bt-corn is not likely to pay a dividend in three out of every four years in Indiana. The researchers discuss a variety of factors such as planting date, level of infestation, yield potential and corn prices that farmers should take into account when making the decision whether to plant a Bt-corn hybrid. The message is clear - there are circumstances in Indiana where farmers are wise to pay the extra cost for Bt-hybrids but many more acres are planted to Bt-corn than can be justified by economic returns.

Field experience with both herbicide tolerant and Bt-transgenic varieties led to an important insight - the value added by input traits is bounded by a variety of factors. Under conditions of high pest pressure or in regions where other technologies or solutions are not viable, transgenic varieties can offer farmers new tools that are worth their added cost. But when these varieties are marketed as near-universal “magic bullets,” many farmers end up paying more and getting less in return. Plus, over-reliance can set the stage for resistance and other longer-term problems.

### **Public Sector Priorities**

Biotechnology research now dominates work in most biological science departments at land grant universities. A 1996 Iowa State study showed that public sector plant breeding research fell 2.5 scientist-years per annum from 1990 to 1994 (Frey, 1996). Most faculty in entomology, plant pathology, weed science, agronomy and horticulture departments are either pursuing biotechnologies or carrying out research on how to integrate them into contemporary farming systems. A small but growing number of scientists are working on developing methods to understand their environmental and ecological impacts. Few are left to study alternatives and system-based solutions.

Funding shortfalls in public universities have made faculty and departments more dependent on carrying out work that the private sector is willing to support directly, or

research that is likely to lead to patentable discoveries that might generate a royalty income stream. In either event, increased biotech-focused effort has come largely at the expense of traditional and applied field research on the interactions of farm system management, resources, pests and crop genetics. The shift is ongoing. A new Dean of the College of Agriculture at the University of Minnesota decided recently to expand agricultural genomics and biotechnology research and plans to do so in part by cutting funding that supports the Minnesota Institute for Sustainable Agriculture, the Center for Alternative Plant and Animal Products, and the Water Quality Center.

This proposal has caught people's attention in St. Paul and a campaign is taking shape to block the shift in resources. The basic argument against the shift is that research priorities on campus are already far too heavily tilted toward molecular biology and "quick-fixes" of problems with high-input agriculture. The debate could grow spirited because of the large and well-organized community of farmers, scientists and activists working to promote sustainable agriculture in the State. The Dean's proposal might have the unintended but constructive consequence of bringing into the open a long-simmering debate on the mission of land grant universities in general and the University of Minnesota in particular.

## **E. Conclusions and Key Steps to Build Public Confidence**

Many biotechnology promoters argue that there are fundamental differences between Europe and America relative to public attitudes on biotechnology. These conclusions are, in my judgement, based on a combination of sloppy and/or biased survey techniques and wishful thinking. Recent surveys, including some carried out by the food industry, show clearly that as Americans learn more about biotechnology and GMO foods, their skepticism grows.<sup>5</sup> Given what emerging science and field experience are telling us about the benefits and potential risks arising from GMO food technologies, consumer and farmer skepticism may soon turn to anger and activism. It already has on Wall Street.

Many biotech promoters are fighting back. Almost daily both the lay press and science journals contain new sweeping pronouncements and guarantees that "all's well" with the biotech revolution. In the last few months, triggered in part by events in Seattle during the WTO meeting, companies have financed new PR campaigns and are working to undermine individuals or groups that have raised questions about the safety or benefits of biotechnology. Politicians have entered the fray. An otherwise even-tempered and thoughtful member of the U.S. Senate has said recently that all evidence of GMO ecological or health risks is "hogwash."

Few people find such responses persuasive. Indeed, such statements tend to just harden public concern, reinforce simplistic notions regarding the extent of safety

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<sup>5</sup> To review results and discussion of several recent surveys, see the Consumer Choice section on Ag Biotech InfoNet at [http://www.biotech-info.net/consumer\\_choice.html#surveys](http://www.biotech-info.net/consumer_choice.html#surveys).

assessments in the U.S., and embolden activists. Still, much of the industry is stuck in the denial phase of grieving over the now irreconcilable breach between the vision and realities of agricultural biotechnology.

More rocky ground lies ahead and the industry and GMO technologies will likely incur added costs and face new hurdles. The costs associated with insuring against and dealing with liability for problems in the field is an example of what could become a significant new cost-center for agricultural biotech pioneers. It is important to add that a full accounting of developmental, regulatory, product stewardship, labeling, marketing and liability associated with most agricultural biotechnologies is yet to be completed. But when things settle down, total costs are likely to prove sobering for much of the industry. The value added by most current GMO technologies is already stretched to the breaking point. People battling a disease may be willing to pay twice or three times more for an improved treatment or more effective drug, but very few farmers will, because first they won't be able to afford such a jump in cast costs and second, they will almost always have and pursue cheaper alternatives

The only way to reduce such costs is to earn public confidence through independent research and thoughtful, thorough and transparent assessment of the benefits, costs and risks posed by given technologies. When risks are documented, companies and/or government agencies must take decisive and prudent action to avoid or limit problems, even in the absence of all the data risk assessors would like to have. In moving ahead with transgenic technology, risk assessors must factor into the equation their lack of understanding of how ecosystems and organisms might adapt. Precautionary approaches that include careful monitoring of actual field impacts for the first few years after commercialization are critical.

Assurances of safety based on an absence of evidence of human health problems and Food and Drug Administration "approval" of existing GMO foods are not convincing. I know this assertion is contentious, but before you dismiss this judgement as ill-informed, biased, or paranoid, read for yourself the views of several FDA scientists in the early 1990s as they developed the agency's "Statement of Policy" and other documents on GMO foods. Several such documents were obtained under the Freedom of Information Act and lie at the heart of the lawsuit against the FDA brought by the Alliance for Bio-Integrity. A set of documents has been posted on the Internet at <http://www.biointegrity.org/FDAdocs/index.html>. They make for interesting reading.

Over the next several months and perhaps years there will be a series of analyses and news reports triggered by this litigation. Many will contrast the technical concerns raised by FDA scientists in the 1991-1992 period with actual FDA decisions and actions. The more thoughtful pieces will also assess recent science to see what it has to say about the risk concerns identified by FDA scientists. Based on my review of dozens of key research reports published in recent years in several fields, many of the scientists' concerns have been borne out and indeed in many respects reinforced. Put another way, it is getting harder and harder to argue with a straight face that scientific evidence

published in recent years resolves all the concerns raised by FDA scientists in the early 1990s.

For these reasons, changes in FDA policy and procedure should be expected. The process of policy change could start the process of calming public concerns, especially if coupled with both increased public funding in essential areas of research and labeling of products now in the marketplace. If the policy reform process remains as contentious as it has been in recent years, it will progress slowly and satisfy no one.

### **Some Suggestions**

Several steps in addition to FDA and USDA policy reforms and more public sector research will be needed to restore farmer and public confidence in agricultural biotechnology.

Companies need to stop marketing GMO varieties as stand-alone solutions to complex problems with roots in farming system design and management.

Marketing programs must emphasize when it is appropriate *and inappropriate* to select a transgenic variety, as well how the technology needs to be used to avoid resistance and adverse impacts on non-target organisms, limit the chances of gene flow, and assure solid economic returns to farmers.

Both government and the private sector must more candidly and thoughtfully describe the limits of genetic technologies and gaps in understanding of potential risks. This need not stop a technology in its tracks but should lead to incremental introduction and trigger field monitoring and research on impacts.

Scientists and regulators must be challenged to develop ways to distinguish almost assuredly safe and beneficial applications of transgenic technologies from those that raise significant risk concerns or offer dubious, at best short-lived benefits. There seems an ample enough supply of the former, promising applications, to justify delaying the commercialization of the risky ones.

Acknowledging that there are legitimate risk-related questions is a first step. Funding independent researchers to pursue answers is a necessary second step. Scientists carrying out this work must be provided access to the tools and technologies needed to really understand how a plant or animal has been genetically transformed. They must not be punished personally or professionally if and when their results reinforce concerns, raise new questions, or point to the need for regulatory restrictions.

Ways must be found to overcome the adverse impacts of patents and intellectual property policies on the conduct of science and the exchange, use, and improvement of germplasm. Fairness issues also must be dealt with. The general public and world community has come to accept great disparity in wealth and income but the same cannot

be said about access to and control over seeds and genetic resources.

Pesticide companies with significant seed industry holdings bear a special burden to assure that their R+D and breeding priorities are not excessively weighted toward transgenic technologies linked to sale of their proprietary products in contrast to other solutions. Their actions and annual seed offerings will be carefully monitored in this regard.

Agricultural biotechnology and genomics have gotten off to a rocky start. Its promise is now held hostage by problems the industry has largely brought upon itself. The credibility of both the U.S. government and industry is on the line, as is the public's soft spot for farmers and the economic performance of major sectors of the U.S. food system.

Shifting gears in the current climate will require diplomacy and leadership. I applaud those in the biotechnology industry, agriculture, government, and the environmental and consumer communities who have started the process. Perhaps the single most constructive next step will be reaching agreement on at least some positive directions and applications and assuring that resources are invested in pursuing them.

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