Principles Governing the Long-Run Risks, Benefits, and Costs of Agricultural Biotechnology

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Public concern and controversy over agricultural biotechnology has triggered a debate around the world on the future applications of molecular genetics and biotechnology to food and fiber production. This debate is overdue and may still prove constructive in the long run. The underlying issues are what kind of food, and food system, do people want and will biotechnology move us in a positive direction?

The strengths and weaknesses of food systems obviously depend greatly on where one sits at the table. In the North, abundance and choice are taken for granted. Food is affordable for most people, despite the fact the average American spends more per calorie consumed than well over 95 percent of humanity. The average share of per capita income spent on food in the United States is the lowest in the world because America is such a rich country, not because food is cheap.

In the developed world, safety, quality, and convenience shape the market place. In the developing world, rural and urban poverty is the dominant cause of hunger. Food insecurity is driven by poverty more so than inadequate production. In India there are millions of underfed people and millions of bushels of surplus grain in storage. The rural poor with access to land will be helped somewhat by improved farming technology, as will the urban poor if supplies increase and prices fall as a result of new technology. But for agriculture and rural economies to become more productive, improve farm family economic status, and do a better job conserving natural resources, prices for basic agricultural commodities simply have to go up. New technology in the absence of policy and market reforms will likely make matters worse for many of the people most in need of a lift from poverty's grip. As U.N. Secretary General Kofi Annan and others have argued recently, cutting back markedly on developed world farm subsidies is urgently needed to help both the urban and rural poor in developing countries.

Over one-third of the cost of producing corn in the U.S. comes from government payments; the figure is somewhat higher in Europe. The price of rice in Japan is ten-times the world market level. Excessive farm sector subsidies in rich countries are flooding the global market place with surpluses, depressing prices and undercutting the ability of poor farmers to improve their economic and food security.

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The global debate over how agriculture and food systems can better meet people's needs is passionate and often muddled. It is easy to get lost in the complex interactions between the many forces that shape the system. Views differ widely over what is right and wrong about the system and the direction it's headed. People see the risks posed by farming systems and technology very differently. Some think biotechnology is the ultimate answer, while others see it as unsafe, unneeded, and even unethical. Given that perceptions of the impacts, risks, costs, and benefits of agricultural biotechnology are so divergent and visceral, it is little wonder that consensus remains elusive when discussions turn to how policy, development assistance, or research capital should be directed and invested. As long as the current state of affairs persists, companies, governments, and international organizations will struggle to find a safe path through the minefield that has become public discourse on agricultural biotechnology.

To move forward, more diplomacy and a new ways to talk about biotechnology are needed. Hardliners on both sides of the debate need to back off extreme and unscientific positions – all biotech is good, wonderful and proven safe; all biotech is too risky and only good for agribusiness.

Reasonable people can and will continue to see the risk-benefit equation differently for a given application of biotechnology. That's a given. What remains unclear is whether reasonable people might also one day agree on certain applications that should move forward, at least under some conditions. For this to happen we need to change the focus and tenor of debate. It must become safe for open-minded people to move out into the agricultural biotech minefield. At least some who do so must survive the exercise and be willing -- and allowed by their employer and professional community -- to explore the landscape a bit further the next time an opportunity arises.

A first step in changing the terms and hopefully tenor of debate is to seek a common understanding of the characteristics of agricultural and food system technologies – whether chemical, biological, or genetic -- that should determine placement on a list of priorities. As a society, we cannot afford to develop, test and commercialize all technically plausible applications of biotechnology. Priorities must be set, choices must be made. A method is needed to screen and rank potential applications. Some will emerge as clearly needed, feasible, likely to be safe, cost-effective, and compatible with cultural values, while a few others, upon reflection, will be seen as too risky or not worth the cost and effort required to bring them to market.

Here, I describe a set of "first principles" against which technology can and should be appraised. These principles encompass performance attributes related to how a technology is intended to work, as well as the technology's impacts and consequences. No technology – whether biotech-based or organically approved – will possibly be fully compatible with all relevant principles and performance attributes. The goal is to work toward more assuredly safe and beneficial technology, while avoiding technology with foreseeable pitfalls and adverse unintended consequences.

Why are "First Principles" Needed?

Secure and sustainable food systems in a country or region must accomplish two things. First, adequate supplies of safe, nutritious food must be produced and accessible to all people, with most of the supply of food coming from regional production or economically sustainable trade. Second, food must be produced without undermining the human communities and farm labor force, as well as the genetic, soil, and water resources on which agricultural production depends.

Principles, performance parameters, and evaluation criteria are needed to determine the degree to which a given technology, practice, or system will contribute to these two fundamental goals. Eleven "first principles" follow in three categories –

- Tactical Choices.
- Management and Problem Solving.
- Equity and Outcomes.

The purpose of trying to reach agreement on "first principles" is to create a mutually acceptable framework within which agricultural technology, systems, and practices can be evaluated. Tactical principles and performance attributes focus on how a technology or system achieves its stated goal – e.g., poisoning a pest with a chemical or biological toxin, versus disrupting pest reproduction or development.

Management and problem solving principles encompass where and how a technology allows or helps a farmer to intervene in the crop or animal production cycle, as well as a technology's impacts on management flexibility and a farmer's ability to innovate. Equity and outcome principles and attributes address the nature and distribution of benefits, risks, and costs, and the scope and reversibility of potential unintended consequences.

First principles should be used to evaluate all agricultural technologies and food system issues, not just biotechnology. First principles are equally applicable to policy and technology choices in the North and South, and to biotechnologies and organic production methods and systems. The weight placed on various principles and performance parameters will appropriately vary by region and in accord with current agricultural and food system challenges, resources, capabilities, and cultural values. Not all principles will be relevant or important in assessing a given type of technology. Uncertain impacts will inevitably be part of the equation and trade-offs across principles will arise.

Applying these eleven "first principles" to a list of technology options should help a country, company, NGOs, or research institutes distinguish technologies that should be pursued aggressively, versus explored hopefully, versus shelved indefinitely. As the most promising, least risky applications are pursued, important experience will be gained and knowledge of natural systems and interactions will deepen, setting the stage for progress to accelerate and broaden.

Tactical "First Principles"

Two principles should guide perhaps the most strategically important set of decisions any farmer, society, scientist or company faces -- "What to produce?" and the related question, "What to research?"

- **Promote diversity**.

  In promoting diversity, attributes and evaluation criteria include:

  Crops, livestock, technologies, and practices should have potential to diversify diets, production systems, and income opportunities.

  > * Those that do not should be assessed more critically on agronomic, pest management, and economic grounds.

  Promote the biodiversity of soil microbial communities and above ground invertebrates to maximize biological control opportunities, and to augment nutrient cycles and flows.

  Diversify the range of tactics and practices used to suppress pest populations.

- **Understand and work within natural limits**.

  Attributes and evaluation criteria include:

  Crops and livestock should be indigenous to and/or likely to adapt well to a region's climates, soils, and pest complexes.

  Production goals must be realistic and sustainable in light of the availability and quality of production inputs – soil, nutrients, genetics, water, sunlight, and human capacity to accomplish field tasks.

  Overcoming one yield constraint almost always creates others. The likelihood and costs of overcoming secondary constraints should be projected and taken into account in setting realistic yield goals.

Management and Problem Solving "First Principles"

Once decisions are made regarding what crops and livestock to produce or conduct research on, or to favor via policy reform, attention must turn to farming system design and management. Five principles are key in evaluating whether technologies, inputs and practices are likely to be part of sustainable solutions.

- **Target solutions at the root of problems.**

  Attributes and evaluation criteria include:

  Prevent problems rather than treat symptoms. Eliminate or counteract the circumstances and biological interactions that give rise to problems.

    Plant breeders should focus on problems only genetic improvement can realistically address. In general, genetic solutions should not be relied on to fix management problems.

    Pest management practices and tactics should focus on population suppression through multitactic Integrated Pest Management (IPM) systems, rather than killing pests with synthetic or natural toxins when and where pests exceed damage thresholds.

- **Incrementally improve, or at least sustain soil quality and productivity.**

  Technologies or systems must not increase soil erosion, worsen compaction or water logging, or lead to or exacerbate natural chemical or mineral imbalances in the soil. The return to almost all investments in agriculture is ultimately bounded by soil quality.

- **Tighten and calibrate nutrient cycles relative to crop needs.**

  Technologies, practices or inputs should not result in or depend upon periodic excesses of nutrients or water compared to crop or livestock needs, nor should they create new leaks or losses in nutrient cycles.

- **Preserve capacity to adapt and innovate.**

  As experience is gained with a technology, practice, or input, farmers should be able to continuously experiment with and improve the ways it is used.

  Technologies, practices and inputs should be amendable to change by farmers to best match unique local conditions and should not reduce degrees of freedom in farming system design and management.

- **Exploit free ecosystem services.**

  Technologies should enable farmers to actively manage and/or more cost-effectively take advantage of free ecosystem services with potential to support crop and animal production and/or contribute to soil fertility and quality.

Technologies that undermine or erode free ecosystem services should be held to a higher standard of agronomic and economic performance.

- **Favor self-sustaining solutions.**

  Ideally farmers should not have to purchase the same inputs or use the same practices every year to address a given production problem. They should have the capacity to replicate and improve upon a technology.

<u>Equity and Outcome Related "First Principles"</u>

Technical possibilities in the world of agricultural biotechnology are exploding at the same time market and consumer acceptance is imploding. Strong medicine is going to be needed to turn this situation around. Risk adverse countries and skeptical consumers will need to see clear evidence that a technology will deliver meaningful benefits, and not just to companies and owners of intellectual property rights. Risk assessment tools, science, and rigor must steadily improve, especially in countries like the U.S. that have embraced "substantial equivalence" and as a result, ignored risk assessment challenges.

- **Assure a sound match between the attributes, requirements, and impacts of technology and the needs and capabilities of intended beneficiaries.**

  For developing world applications, technologies that increase routine reliance on purchased inputs and/or require technical skills and capabilities not currently in place should be avoided.

  The capacity to manage potential ecological and food safety risks and impacts must be taken into account in risk-benefit projections.

- **Avoid external costs and risks.**

  Inherently hazardous technologies and inputs should be avoided, as should those that place markets and essential production tools and natural resources in jeopardy.

- **Do No Harm.**

  Ideally, the consequences following adoption of a technology, practice, or input should be predictable and benign. To the extent consequences are impossible to project, a more cautious, incremental approach should be taken.

  Prevent the emergence of new pests and/or slippage in pest management systems by minimizing selection pressure across time and space.

- **Promote equitable distribution of income streams associated with agricultural production.**

  Technologies or inputs that increase the profitability or economic status of consumers or private companies at the expense of poor and relatively disenfranchised farmers should be avoided.

Applying the Eleven Principles to Selected Technologies

A variety of qualitative and quantitative methods could be used to apply these eleven principles, or some other set of principles, to contemporary agricultural technologies. Ranking technologies against these eleven principles is not a substitute for rigorous environmental and food safety risk assessments, but rather an exercise to determine which technologies are worth moving forward with, possibly to the point where a full risk and benefit assessment can be completed.

There is no intrinsically correct way to apply these or any other set of principles. The methods used and weights applied to various principles will obviously impact the outcome. Companies, investors, regulatory agencies, international organizations, professional societies, research organizations and interest groups have their own, or are developing methods to compare agricultural technologies. Most share at least some common elements.

It goes without saying that no one has the right to impose their personal values and priorities on others. Still, unless we are happy with the status quo, we must reason together and try to move the debate forward. Toward this end, a brief discussion follows of some of today's major agricultural biotechnologies relative to their compatibility with the above described first principles.

The two major agricultural biotechnologies in use are herbicide tolerant plants and plants engineered to express *Bt* endotoxins in their tissues for control of certain insect pests. Despite market success in the U.S. and a few other countries, these technologies remain controversial. Why?

Herbicide Tolerant Crops

Herbicide tolerant plants, particularly Roundup Ready soybeans, have greatly simplified weed management. In some areas, adoption rates are very high and in Argentina, approach 100 percent (Benbrook, 2002).

As currently used in the U.S. and Argentina, herbicide tolerant (HT) soybeans have limited crop diversity somewhat by increasing soybean acreage. The expansion of soybean farming onto previously forest and rangelands has clearly reduced local biodiversity (Benbrook and Baumuller, 2003).

More seriously, the technology is designed to, and clearly does increase reliance on one weed management tool – herbicides. Moreover, it has increased dependence on a single herbicide, glyphosate (Benbrook, 2001). Excessive reliance on any single pest management tool heightens the selection pressure imposed on pest populations and sets in motion evolutionary processes that ultimately will undermine efficacy (Lewis et al., 1997). Hence, it is no surprise that Roundup resistant weeds have evolved in the U.S. and are beginning to force farmers to add additional herbicides to their control programs.

In the absence of a concerted pesticide-industry wide glyphosate resistance management campaign, the efficacy of this technology will be incrementally eroded. No one knows whether it will take five or 15 years for this process to unfold. How the industry and farmers respond will surely impact evolutionary dynamics.

The emergence of Roundup resistant weeds raises a key point and caveat. Problems with resistance and weed shifts are an adverse impact triggered by how HT technology is used, and are not inherently inevitable based on the properties of the technology. The same is true of resistance to *Bt* and *Bt* transgenic crops, as well as genetic resistance to any pest, whether brought about through conventional breeding or biotechnology. How a technology is deployed, in particular how heavily it is relied upon, drives whether potential problems and risks become real ones. Accordingly, it is important to take into account levels of adoption and degrees of reliance in evaluating the impacts of many technologies.

Paradoxically, the best way to maximize the benefits of many individual technologies is to use them sparingly, in combination with other technologies. Many little hammers, used in complex rotations, are far better than one big hammer, especially a big hammer everyone has access to.

Does HT technology target the root of weed management problems? Farmers eagerly adopted HT soybeans to get away from the use of highly active low-dose herbicides in the imidazolinone and sulfonylurea classes (Benbrook, 2001). Herbicides in these families of chemistry were leading, in some circumstances, to crop injury and carryover problems. Herbicide tolerant soybeans seemed a logical solution to carryover problems, but do not address the root of the problem, which is why weeds tend to do so well in soybean fields.

The "Avoid External Costs" and " Do No Harm" principles apply to some HT crops. Research has shown that applications of glyphosate on fields planted to RR soybeans impair root development and the activity of the microorganism responsible for nitrogen fixation by soybean plants (King et al., 2001). Since most cropland producing soybeans in the U.S. contains high levels of nitrogen, RR soybean yields are typically not affected. In drought years, the impact on yields can become significant. Accordingly, this HT technology has a modestly to moderately negative on soil quality and the nutrient cycles. In developing countries where nutrients are not nearly so abundant, the impacts of this unintended consequence may prove more serious.

Much has been said about whether HT soybeans reduce herbicide use and hence, pesticide risks. They clearly do not reduce the volume of herbicide applied, since glyphosate is a relatively high dose herbicide. The planting of RR cultivars has dramatically decreased use of low-dose herbicides that pose production-oriented risks to farmers. This shift has benefited farmers who choose to largely rely on herbicides for weed management. But HT technology in the U.S. has not resulted in significant benefits to the environment or society as a result of reducing pesticide use, nor has it created significant new risks, other than the emergence of resistance.

The most substantial potential benefit of HT technology stems from its compatibility with no-till production systems. If HT varieties were predominantly planted using no-till systems on highly erodible land, the public benefits would be unequivocal. Resistance would still need to be managed, as would other environmental impacts, but the steps needed to do so would be more than justified by the reductions achieved in soil loss and sedimentation. This is not how HT technology has been marketed or adopted, however. HT soybeans have had a very modest impact on adoption of no-till and conservation tillage, and there has been near-zero effort made to target the technology to highly erodible lands.

Economically, HT technology has been about a wash for farmers, not because the technology is inherently efficient or increased yields, but because the price of glyphosate and other herbicides has dropped about one-half on average since the introduction of HT soybeans. The price of glyphosate fell because it went off patent and generic competitors entered the market. Manufacturers have also markedly cut the prices of other herbicides in an effort to slow their loss of marketshare to glyphosate products.

In the U.S. biotechnology companies have charged a technology fee and/or price premium for GMO seeds roughly equal to the perceived average economic advantage of the added trait to the farmer. Many farmers with serious weed management or Lepidopteran insect problems benefited substantially from the planting of GMO seeds; farmers who were managing these pest problems effectively with other technology and/or systems typically had little to gain economically from HT or *Bt* crops. Most who switched did so to simplify their production systems and minimize a problem-area that required considerable management attention.

A growing concern in farm country is what happens if the RR soybean system no longer works because of weed shifts and resistance. This technology has increased farmer dependence on seed-biotech-herbicide companies. Perhaps equally effective, affordable replacement technology will reach the market as the efficacy of RR technology declines. But if it does not, both the cost and difficulty of managing weeds in soybeans will increase, at least until farmers gain access to, and become skilled in the use of alternative technology or systems. The fact that HT technology has markedly reduced farmer use of non-chemical alternatives and undercut promising research in multitactic integrated weed management systems works to perpetuate farmer-dependence on herbicides. Some people view this as an inherent disadvantage and others couldn't care less how weeds are managed in soybeans.

Bt **Cotton**

The benefits of *Bt* cotton have received much attention in the wake of the Qaim-Zilberman piece in *Science*, "Yield Effects of Genetically Modified Crops in Developing Countries" (Qaim and Zilberman, 2003). *Bt* cotton works well in controlling several major Lepidopteran insect pests, as shown repeatedly in grower fields and research trials in several countries. The article's conclusion that *Bt* cotton will increase cotton yields 60 percent to 80 percent in developing countries, and sometimes 100 percent, is extrapolated from limited company field trials in a year with intense insect pressure. The article acknowledges that in plots planted to conventional seed with standard insect pest management practices, losses were about 60 percent of yield. By eliminating most of such loses, *Bt* cotton or other alternative technology would double yields.

The suggestion that all farmers have to do to achieve such huge yield increases is to plant *Bt* cotton assumes there are no other constraints to yields, nor other effective insect pest management options. Both assumptions are implausible and have been challenged by entomologists in India, including some who support development of transgenic technologies (e.g., see Sahai and Sen comments in the March 5, 2003 "Special" issue of AgBio View).

Still, providing access to safe insect pest management technology via seed is highly desirable as a general goal, and indeed is the focus of a major share of conventional plant breeding effort. But delivering lethal doses of a natural toxin like *Bt* through plant tissues will lead to many of the same problems as chemical sprays, as pointed out by U.S. Department of Agriculture scientist Dr. Joe Lewis and colleagues in their seminal 1997 *Proceedings of the National Academy of Sciences* paper "A total systems approach to pest management" (Lewis et al., 1997). In this paper, the authors state:

> "The use of therapeutic tools, whether biological, chemical, or physical, as the primary means of controlling pests rather than as occasional supplements to natural regulators to bring them into acceptable bounds violates fundamental unifying principles and cannot be sustainable."

In addressing emerging applications of biotechnology to pest management, they argue that:

> "As spectacular and exciting as biotechnology is, its breakthroughs have tended to delay our shift to long term, ecologically based pest management because the rapid array of new products provide a sense of security just as did synthetic pesticides at the time of their discovery in the 1940s….the manipulated pathogens and the crops engineered to express toxins of pathogens are simply targeted as replacements for synthetic pesticides and will become ineffective in the same way

> pesticides have. It will be unfortunate if these powerful agents are wasted rather than integrated as key parts of sustainable pest management systems."

They cite the basic tenets of ecologically-based, or biointensive Integrated Pest Management (IPM) in arguing that the most desirable pest management technologies, in terms of costs and risks, will trigger or reinforce natural cycles, developmental processes, and multitrophic interactions that work to sustain balance among pest and beneficial organism populations in natural systems.

Bt crops do not do so. As Lewis et al. point out in comparing foliar insecticides to *Bt* crops, the transgenic approach "…amounts to a continuous spraying of an entire plant with the toxin, except the application is from the inside out." A crop genetically engineered, or conventionally bred, to over-express jasmonic acid when attacked by caterpillars, or other chewing or sucking insects, would be consistent with this basic principle (Seo et al., 2001). Such over-expression can attract parasitoids that in turn lessen insect feeding damage (Thaler, 1999; De Moraes et al., 1998).

Where insects susceptible to *Bt* have driven onfarm insecticide use, cotton farmers growing *Bt* cultivars have been able to markedly reduce applications of typically high-risk, broad-spectrum insecticides. Encouraging and important recent research in Arizona has shown that where 65 percent or more of the cotton acreage has been planted to *Bt* varieties, area-wide suppression of the pink bollworm has occurred (Carriere et al., 2003). This is a positive development for several reasons.

In Arizona, *Bt* cotton has eliminated the need for most applications of broad-spectrum insecticides on cotton, giving populations of beneficial organisms a chance to rebuild. These populations are now starting to make important contributions in suppressing several potential insect pests, including the pink bollworm (Carriere et al., 2003).

Area-wide pest suppression of pink bollworm populations could also allow farmers to better manage resistance. As populations decline, it will be possible for farmers to periodically forego the planting of any *Bt* cotton in an area. Reduced risk insecticides, coupled with multitactic IPM, will be effective in such years, and can be augmented late in the season if needed by a broad-spectrum insecticide. The elimination of any *Bt* selection pressure for a whole year will surely increase the effectiveness of ongoing Resistance Management Plans (RMPs). Whether this new understanding of the impacts of *Bt* cotton will be taken advantage of in strengthening area-wide resistance management remains to be seen.

Vitamin Enhanced Crops

Rice engineered to produce higher levels of Vitamin A has been one of the most widely debated applications of agricultural biotechnology. Recently, a method has been found to increase the Vitamin C content of crops by increasing the expression of the enzyme responsible for recycling ascorbate (Chen et al., 2003).

The evaluation of these technologies is underway, with Vitamin A rice much closer to possible commercial adoption than Vitamin C enhanced crops. Some people still question the wisdom of enhancing vitamin content through genetic engineering. Those questioning such technology usually argue that there are other, simpler, less costly ways to increase vitamin consumption. They project that more progress would be made in solving the underlying problem – vitamin deficient diets -- if the resources required to bring transgenic vitamin enhanced crops to market were instead invested in efforts to improve the agronomic performance of vitamin-rich, locally grown fruit and vegetable varieties.

It is hard to imagine how anyone, or any analysis, could definitely prove or disprove these projections and assertions. Still, a degree of diversity in R+D efforts addressing a given problem is intrinsically beneficial. If one accepts this "don't put all eggs in one basket" principle, then ideally the substantial new investment in the development of transgenic vitamin enhanced plants in the last decade has been or will be accompanied by increased investment in efforts focused on achieving the same goals through other means.

In terms of the safety evaluation of these two technologies, Vitamin A rice may raise more food safety and agronomic performance issues than Vitamin C enhanced crops. This is because two biosynthetic pathways novel to the rice genome must be moved into rice cultivars to increase Vitamin A content, whereas it appears possible that Vitamin C content might someday be enhanced simply by changing the expression level of enzymes already produced by plants. Differences between the scope of genetic modification required to add a given trait to a crop is highlighted in a recent article in *Nature Biotechnology*, "Transgenic Organisms – Time for Conceptual Diversification?" (Nielsen, 2003). Nielsen points out that "The extent to which transgenic organisms differ from traditionally bred organisms underlies much of the controversy surrounding the use of GMOs..." and that:

> "Current approaches to gene technology assisted breeding have been called 'brute-force' in their use of distantly related genes with little consideration for the multiple evolutionary changes that have occurred in the biochemical networks separating species."

Leveraging Local Knowledge and Indigenous Resources Via Biotechnology

Transferring developed world biotechnologies like HT and *Bt* crops to developing nations is almost certainly not the best way for resource poor, food insecure countries to benefit from biotechnology.

Recognition and acceptance of what biotechnology can and cannot do in promoting food security is a critical missing ingredient in contemporary debate. Too many biotechnology "true believers" appear to only see transgenic solutions, regardless of the nature of a problem. In their zeal to promote biotechnology as the one true path, they sometimes discount or outright dismiss the actual and potential contributions of other problem solving strategies, approaches, and systems-based technologies. For example, a prolific proponent of biotechnology wrote in a post to Ag BioView that:

> "Not too long ago, it made sense to argue that 'native Mexican landraces' needed to be preserved because of their 'biodiversity' and the 'possible benefits' that might lie undiscovered in their germplasm. Seeds from these various landraces are held by CIMMYT at great expense, and are about to become obsolete and worthless.
>
> "Yes, that's true. Obsolete and worthless. The more advanced the knowledge of gene function and transfection becomes, the more pointless 'biodiversity' and seed banks become. Seed banks and biodiversity are only important if your only available technology is conventional breeding….Ten years from now, the expense for seed banks will be deemed pointless, their contents will be fed to cows and pigs…" (Aple, 2002).

Such unbounded confidence in the power of biotechnology worries many people. It worries me. I am excited by the power of biotechnology and accelerated scientific discovery, but do not foresee biotechnology rewriting the laws of nature or making germplasm obsolete. I cannot imagine how it will render soil fertility or ecological sound approaches to pest management irrelevant.

For biotechnology to be a part of sustainable solutions, it's power must be directed, at least for the foreseeable future, toward helping farmers more effectively manage natural systems, cycles, and interactions, rather than efforts to work around, supplant, or overwhelm them.

Moreover, the benefits of new technology are too often eroded or overwhelmed by the impacts of bad food and farm policies and failure to support rural development. Dr. John Kilama, CEO of the Global Biodiversity Institute and a former Dupont scientist, echoed this theme in remarks on the recently announced "African Agricultural Technology Foundation":

> "The initiative is not getting to the core of the problem in Africa. I wish people would focus seriously on how to change governments in Africa. I'm a strong proponent of biotechnology, but other things need to be done that are more critical than giving seeds to farmers." (Suh, 2003).

Moving Forward in Addressing Food Security Needs

There is wide agreement that instead of focusing on western world commodity crops (corn, soybeans, cotton, and wheat), emphasis should be placed on nutrient dense crops that are currently key foods in developing countries – e.g., cassava, millet, pulses, bananas, beans, and squashes. While it is important to focus on food crops, altering plant genomes is only one way to increase crop productivity and prevent pest losses.

In some cases, the most direct, affordable benefits from biotechnology might come from altering soil microbial communities in ways that directly benefit plants. The identification and/or improvement of beneficial soil amendments, compost inoculants, and seed treatments sometimes will prove a relatively easy and quick way to increase production.

In order to better manage plant diseases, many teams are working to genetically engineer plants to augment systemic acquired resistance (SAR), the plant's generic immune response to many pathogens. In 1997 a team based at the University of California-Berkeley described the role of the NDR1 gene in controlling SAR (Century et al., 1997), an important breakthrough that dramatically increased research interest and funding. Several teams have since been pursuing what is sometimes called the "master switch" for plant defense mechanisms (e.g., Verberne et al., 2000).

While most of the excitement in the plant science community and new money for combating plant disease has gone to work on triggering or reinforcing SAR via genetic modification, field research in China in 1998-1999 produced dramatic and encouraging results through an approach to disease management called intraspecific crop diversification (Zhu et al., 2000). Rice fields in five townships were planted to a mixture of rice cultivars that were susceptible and resistant to rice blast disease, the region's major pathogen. Yields rose 89 percent and blast severity fell 94 percent in the fields planted to seed mixtures compared to monoculture controls. The authors note that:

> "…it is significant that the diversification program described here is being conducted in a cropping system with grain yields approaching 10 Mg ha^{-1}, among the highest in the world. The value of diversity for disease control is well established experimentally and diversity is increasingly being used against wind-dispersed pathogens of small grain cereals."

In the future, low-cost and effective disease management strategies in some row and grain crops may depend largely on the planting of diverse mixtures of cultivars. Biotechnology may play a supportive role in making this strategy feasible by helping produce varieties that yield compatible grain, and grow and mature in unison, allowing efficient harvest. Both transgenic tools and marker-assisted breeding could play a role in developing such commercially matched, but genetically distinct varieties. This sort of strategy, where plant breeders focus on relatively modest changes in cultivars to better exploit an existing, ecosystem-based pathogen control mechanism, is consistent with the conditions for pest management sustainability set forth by Lewis and colleagues in their seminal 1997 *Proceedings of the National Academy of Sciences* article (Lewis et al., 1997). It is also striking how different this approach is conceptually to ongoing efforts to trigger or reinforce SAR.

If it appears a toxin is needed to poison an insect, the first preference should be to identify an indigenous biochemical that is effective in disrupting pest reproduction, feeding, or development, modes of action that tend to require far less "killing power" and greater species-specificity than traditional insecticides. Then, options to extract or produce such biochemicals cheaply and locally should be explored. In some cases, relatively simple methods such as fermentation or composting will be cost-effective and accessible to small scale, resource poor farmers. Alternatively, a synthetic analogue of the material may need to be produced and purchased. Developing a source of the biochemical that can be sprayed or otherwise applied to a field will provide farmers the opportunity to practice biointensive IPM – scouting pest levels and applying pesticides or control interventions only when and where needed. This approach can save much time, effort, and money.

Developing a transgenic cultivar expressing the biochemical should be viewed as an extreme response and last resort. When farmers' rely on transgenic cultivars, they treat pests prophylactically. Pests are subjected to selection pressure even when pest populations are below damage thresholds. Whenever possible, genetic engineers should focus first on ramping up plant defense and response mechanisms indigenous to plants, as opposed to trying to add wholly new biochemical responses.

Plants produce over 50,000 compounds, with a significant share triggered by pest and abiotic stresses (Dillard and German, 2000). The function of a few thousand are known; great potential awaits discovery of the roles of the rest, since the levels of these compounds should be readily subject to genetic modification. Of course, not all will prove benign when consumed by mammals, but some secondary plant metabolites will prove beneficial. Recent research has shown that plants emit flavonoids when attacked by pests, some of which that have potent antioxidant activity and may help prevent cancer in humans (Asami et al., 2003). When plant breeders manipulate plant metabolites, whether through use of transgenic or conventional breeding techniques, food safety consequences must be thoroughly explored.

If there are vitamin or mineral deficiencies in an area, crops suited to the region with a more desirable composition of vitamins and minerals should be identified. Constraints to wider production of these crops should be assessed and an effort made to overcome them. If increased production is not feasible because of some pest or abiotic factor, steps should be explored to deal with these constraints, including perhaps creating transgenic cultivars engineered to overcome a specific problem. If this and other strategies are too expensive or ineffective, then and only then should the focus turn to moving new biosynthetic pathways into locally adapted plants. This later strategy for addressing the problem of nutritional deficiencies is likely to often be the costliest and most prone to setbacks and disappointments. In the case of a major crop like rice, the potential long-term benefits are also enormous. Finding the right mix and balance of high probability, short-run incremental improvements versus longer-term but riskier and bigger impact R+D investments is an ongoing challenge.

Many applications of biotechnology are envisioned to provide plants a better chance of dealing with problem soils. For example, a team of researchers in Mexico is exploring whether plants engineered to express a citrate synthase gene from *Pseudamonas aeruginosa* will enhance aluminum tolerance (de la Fuente et al., 1997). Aluminum toxicity is a major cause of depressed yields in acid soils and is a particularly serious problem in the tropics, where heavy rainfall and leaching increases acidity.

Whether a soil is plagued by chemical or mineral imbalance, or problems of soil structure, breeding a transgenic plant that is better able to cope with the problem bypasses several other, possibly lower-cost and more sustainable solutions. Three things must happen simultaneously to convert a poor quality soil that is lacking in nutrients and biological activity to a healthy soil capable of supporting good yields on a sustainable basis:

- Whatever is causing the soil to be compacted, imbalanced, waterlogged, or saline must be stopped or altered;
- Soil microbial biodiversity must be enhanced to provide the foundation for deeper nutrient cycles, bioremediation of imbalances, and other essential curative processes; and
- Sources of organic material must be secured and added to the soil to provide food for the organisms that have important work to do.

In some cases, transgenic soil inoculants, or seed treatments, will prove valuable in enhancing soil microbial biodiversity. These can be manufactured relatively cheaply and delivered to the farm via compost inoculants, seed treatments, or soil amendments. Often the only quick way to assure new sources of organic material is to increase the supply of commercial fertilizers. Where fertilizer is scarce or too expensive, soil fertility replenishment methods have to be worked out, based on locally available minerals and organic supplements (Sanchez, 2002). In the end though it is much better to heal a problem soil, especially soils where the problems are man-made, than it is to try to create a transgenic cultivar that does the near impossible – perform well in sick soil.

In the developing world most food-related problems stem from not enough of the essential ingredients of a safe, secure food supply. In the developed world, and surely in the U.S., excesses lie at the heart of our most serious farming and food system problems. We pollute drinking and surface water with nutrients because fertilizer is so cheap and because we have too much manure relative to the surrounding cropland's assimilative capacity.

Our food system supplies the average American adult with 3,800 calories per day (Nestle, 2003) – almost twice the level needed to sustain health for most adults (about 2,000 calories). Sixty-five percent of adults in the U.S. are overweight, nearly a third are obese, and the prevalence of obesity is spreading and becoming more common among children (Hill et al., 2003). The remarkably inefficient utilization of food energy in the U.S. and the growing volume of waste are problems that rarely get discussed. When excess is accepted as a given, almost a birthright, inefficiency becomes an attribute and ironically, a focus of scientific discovery and technical innovation.

Too many animals are crammed together in most confinement operations, where they experience too much stress and are far too dependent on drugs. And as a result, too many antibiotic resistant genes are making the rounds in bacterial populations, finding ways to move from the farm, into the food supply, and then into hospitals, nursing homes, cruise ships, and other environments conducive to their spread in human populations. As a result, more and more people are experiencing serious medical problems from infections that were once easy to treat.

Many applications of biotechnology have been conceived and are being pursued to address America's sins of excess on the farm and in our food system. Phytase transgenic pigs (Golovan et al., 2001) and low-phosphorous transgenic corn are being developed to deal with the swine industry's contribution to water quality degradation. Transgenic vaccines and animal drugs are being developed to protect animals from diseases triggered by how animals are raised. Multiple technologies are being pursued to reduce or alter the fat content of food, or to impair the body's ability to digest food or metabolize energy. The hope driving this work is that Americans can become more effectively inefficient in what we produce, process and consume. In short, we want to keep our bad eating habits but want to be sparred the consequences.

It strikes many people that using biotechnology to "fix" problems rooted in excess is like chasing one's tail. Most suspect there are better ways to solve the underlying problems. Avoiding excesses in our food system and on the farm is not going to happen by divine intervention. It will take a change in policies, prices, and social priorities; it will take straight talk from the government and from health and agricultural professionals. Governments will need to stop investing scarce public resources in farm subsidies that create or worsen surpluses, especially of fat and sugar-rich foods. Better ways must be found -- and the will -- to invest in technologies and food system changes that attack the roots of problems, not their symptoms.

Biotechnology can and will make important contributions to plant breeding and food security, but its benefits have often been oversold and its costs underestimated. Grandiose claims, coupled with the shift of resources and scientific talent away from other ways to solve problems, makes people nervous. A more conservative and disciplined approach in bringing new technology to the market will help counteract these concerns.

People are beginning to appreciate that the impacts of agricultural biotechnologies depend on where and how the technologies are deployed, as much as the intrinsic nature of a given technology. Often, targeting emerging biotechnologies to just certain circumstances is a sound strategy to enhance potential social benefits, while containing risks. Such a modest approach, however, undercuts the typical need for companies to maximize near-term sales, profits, and return on investment.

One necessary step in gaining public confidence will be methods to assure that new technologies are introduced incrementally to the market. Given that risk assessment methods and science are imperfect, systematic and independent monitoring of impacts is vitally needed in areas where a new technology is first adopted. But now, the U.S. and most regulatory systems work like a traffic light – they either restrict technology developers to very small, controlled experimental plots, or open the door to 100 percent commercial adoption.

Instead of trying to find ways to shift developed world applications of biotechnology to the developing world, a sounder strategy might be to survey how the tools of biotechnology might lead to better understanding of the linkages between indigenous resources and knowledge and agricultural production and farm family well-being. Such understanding will surely lead to insights into how to improve pest management, tighten nutrient loops, improve health, and increase yields and hopefully incomes. Over time incremental progress toward these goals may set the stage for more dramatic biotechnology-driven breakthroughs in the future.

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