Can You Get There From Here? Speed Bumps in the Road To Health And Environmental Biotech Applications

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The global division over genetically modified (GM) foods has, by now, assumed a familiar dimension. In the United States and Canada, farmers routinely grow GM varieties of crops and consumers readily (if unknowingly) eat foods containing ingredients derived from GM crops. The US media have paid relatively little attention to GM foods, and while one cannot say that the public has accepted GM foods, it is clear that the majority of US consumers do not view GM foods with active concern. Indeed, the most salient finding of numerous polls is that US consumers remain largely uninformed about GM foods and their presence in the food supply (Hallman, 2005; PIFB, 2005).

The situation is far different in other parts of the world—parts of the world that also happen to be major markets for US farm exports. European consumers in particular are hostile to GM crops and food. Even when approved as safe by European Commission regulators, few GM foods are available for sale in the EU because retailers and manufacturers fear hostile consumer reaction to foods labeled as containing genetically modified organisms (GMOs) (USDA, 2005). As a consequence, the global market for commodities like corn has been divided into GM and non-GM zones, complicating trade. In part because of these trade disputes and market uncertainties, the future for new GM-food crops is clouded.

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The question is whether plant biotechnology[1] can be harnessed to provide benefits outside of the area of food and feed. Can the kind of global deadlock that has emerged from the introduction of GM crops and food be avoided? Is the opposition to the use of plant biotechnology limited to its use in food, or can the potential health and environmental benefits of the next-generation of plant biotechnology change the contours of the global debate? What are some of the obstacles that await the commercialization of health and environmental applications of plant biotechnology?

The temptation to generalize too much should be resisted. Experience and common sense suggest that every application is likely to have its own opportunities and challenges, and across-the-board predictions are likely to be misleading. Some of the issues specific to different types of applications are explored later in this paper. Nevertheless, any new GM plant is likely to have to face four critical hurdles that will require both time and money to overcome on the road to commercialization. Some of these hurdles are no different from those faced by any novel product, while others are unique to products developed through biotechnology. First, of course, is the development of the product itself—proving technical and economic feasibility. Second, products of plant biotechnology need stewardship and management beyond that required for plants developed through conventional breeding, both as a requirement of regulators as well as the necessity of sound business practice. Third, plant biotechnology products need to pass through a regulatory review and approval process that involve both direct and indirect costs. Finally, as with any product, a plant biotechnology product must meet the ultimate marketplace test: are there buyers willing to buy it at a price that delivers a profit to the developer?

The Market Potential of Health and Environmental Biotech Applications

A number of products are being developed through plant biotechnology that could have significant health or environmental benefits beyond food or feed. Understanding what the potential market may be for these applications is an important starting point in understanding the hurdles that they face on the road to commercialization. Other contributors to this volume will develop these points in much greater detail, so only a summary is offered here.

Plant-Made Pharmaceuticals

The potential economic and safety benefits of producing therapeutic proteins from plants have been explored in a number of venues (PIFB, 2002; BIO, 2005a). The market for antibodies is projected to be $26 billion by the year 2010 (Novis, 2005), but current production practices for antibodies cannot keep pace with demand and there appears to be a significant supply shortfall. In particular, the costs associated with scaling up traditional bioreactors using animal or microbial cells create a significant bottleneck in

[1]For the purpose of this paper, the term "biotechnology" is used in the popular (rather than scientific) sense to refer to recombinant DNA techniques. Similarly, the terms "genetically modified" and "transgenic" are used interchangeably and refer to plants modified through recombinant DNA technology to introduce novel or enhanced traits.

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the development of therapeutic proteins. One of the potential advantages of plant-made pharmaceuticals (PMPs) would be the ability to scale up relatively quickly and at relatively low cost. In addition, there may be fewer safety concerns about proteins derived from plants rather than from animal cells.

Unlike food-biotech applications, PMPs potentially distribute benefits along the value chain. For farmers, growing a high-value crop from low-cost commodity species could offer a way to enhance farm income. For consumers, the potential lower cost of therapeutic proteins would be of considerable benefit. For that reason, it is not surprising that the use of biotechnology to create lower-cost pharmaceuticals remains one of the reasons most strongly supported by the US public (PIFB, 2005). The potential application of the technology to develop vaccines that may be of particular benefit to developing countries is also the subject of considerable research and development effort in the non-profit arena (Mason *et al.*, 2002).

Forestry Applications

The application of biotechnology to forestry would also appear to have significant market advantages. Increasing demand for wood and wood products from a growing world population poses a challenge for forestry management and forest-product companies, which are increasingly under pressure to reduce logging in natural forests and to adopt environmentally sustainable practices (Hardaker, 1997; Brooks, 2001; PIFB, 2001). While these pressures have led to the development of forest plantations carefully managed to enhance growth, commercial forestry has not yet captured the benefits of improved genetics that have accounted for significant productivity gains in crop agriculture. The use of biotechnology may provide an opportunity for forestry to make genetic improvements more quickly that could help increase yields by reducing disease, improving pest resistance, and promoting faster growth. In addition, the use of biotechnology to control certain traits more directly could lead to the introduction of trees better suited for processing in specific applications, such as pulp and paper (PIFB, 2001; ArborGen, 2004; El-Lakany, 2004).

The spread of disease among major species of trees in the United States, including elms, chestnuts, oaks and the eastern dogwood, has also created an urgent need to develop disease-resistant varieties. While research using conventional breeding techniques continues, biotechnology may offer a way to introduce desirable disease-resistance traits more quickly (Osusky, 2000; PIFB, 2001; ArborGen, 2004;).

Phytoremediation

The clean up of environmentally contaminated sites remains a huge challenge in this

country. The Environmental Protection Agency (EPA) estimates that tens of thousands of contaminated sites still need clean up in the United States (EPA, 2004). In most cases, the technology of choice is simply to dig up contaminated soil and cart it to some other place. Technologies for treatment *in situ* remain costly and controversial. Phytoremediation offers a number of potential benefits, including lower costs, better performance and greater public acceptability (EPA, 2005). According to EPA (2005), field trials of phytoremediation techniques have reached a promising stage, and estimated costs of various phytoremediation techniques vary from 10% to 50% of physical, chemical, or thermal clean-up techniques. At the same time, phytoremediation is likely to be useful for only a small subset of affected sites where the contaminants lie within the root zone (EPA, 2005). Estimates made in the late 1990s suggested that the domestic market for phytoremediation ranged from $3 million to $30 million, with projections ranging as high as $370 million by 2005 (Kidney, 1997; Glass, 1998). Given this extraordinarily wide range of estimates, it is clear that there is still significant uncertainty about the potential market for the application of phytoremediation, and that much will depend on how well phytoremediation actually performs in-site clean ups. The goal of research is to use biotechnology to develop plants that are more efficient, further reducing costs and potentially decreasing the time it takes to decontaminate a site.

There is still significant uncertainty about the potential market for the application of phytoremediation.

Threshold Question: Who Bears the Cost of Product Development?

Clearly, there appear to be significant market opportunities for applications in these three areas. However, the threshold question faced by any developer is easy enough to state: who is going to pay the cost of taking the product through all of the critical stages of proof of concept, development, testing, regulatory approvals and marketing? For the private sector, products can be self-financed if the developer is a large, well capitalized company with R&D budgets, but small businesses and start-ups will need to look to venture capital and partnerships to sustain them through the development and approval processes.

The willingness of the private sector to invest in product development will depend largely on the anticipated return on investment, which includes not only consideration of potential revenues downstream, but also the costs associated with the process of bringing a product to market. Products that are likely to be commercialized through traditional private-sector incentives are those for which there is a well defined and profitable market. In addition, the private sector will tend to invest in products only where there is strong intellectual-property protection to prevent potential "free rider" and competition problems. On the cost side of the equation, some of the uncertainties unique to plant-biotechnology products make predicting development costs more difficult and raise the risk for investors.

As the history of the development of plant biotechnology demonstrates, many potential applications are unlikely to meet the conditions for private-sector development and investment. In some instances, products may lack a viable market capable of returning sufficient revenues—such as in the case of niche food crops or the development of plants modified to provide vaccines for endemic diseases in the developing world. In other instances, steep development or regulatory costs or uncertainty about market acceptance could deter private-sector development. If products with potential "public" value are going to be developed, they will have to come from the non-profit sectors: government, university, and other non-profit research institutions.

But the non-profit developer faces the same question: where does the money come from to pay the cost of taking a plant-biotechnology product through all the required steps? Since non-profit developers tend to focus on the "public goods" that are unlikely to return a profit to a private investor, they must rely on sources of funding from governments, foundations and other donors. The funding plight of non-profit plant-breeding research in the United States and throughout the world has been well documented (Frey, 1994; Heisey *et al.*, 2001). While most plant breeding used to be in the public sector, private-sector research now dominates as a result of declining public funding and new forms of intellectual-property rights and modern biotechnology that spurred increased private investment (Alston, 2004).

The funding support for plant-biotechnology products that are truly "public goods" remains a serious problem.

Non-profit institutions face additional challenges when it comes to the use of agricultural biotechnology and plant-breeding programs. Such institutions traditionally have little experience with the stewardship and regulatory issues associated with the management and development of bioengineered crops. In an environment characterized by scarce resources, the increased costs and uncertainties faced by products of plant biotechnology also operate as a significant constraint. In some instances, particularly where a product has some potential for commercialization, non-profit organizations may enter into partnerships or licensing agreements with private-sector entities that have more experience in commercialization as well as the management capabilities to deal with stewardship and regulatory issues. However, the interest of the private sector in such partnerships will still be limited by the potential profitability of the product. As a result, the funding support for plant-biotechnology products that are truly "public goods" remains a serious problem.

Speed Bumps in the Road to Market

The threshold question, stated above, is simple: who pays? The next question, of course, is: how much? Surmounting the hurdles of development, management, regulatory approval and commercialization all require investments of time, resources, and money. Having a

clear understanding of those costs is critical to all developers, but is of particular interest to private-sector developers and investors who are making business decisions about whether or not to invest in the technology. Below, the potential costs—and uncertainties—associated with each stage, with reference to health and environmental plant biotechnology applications, are considered in more detail.

Technical and Economic Feasibility

The initial hurdle, of course, is technical feasibility—that is, simply getting the technology to work. It is one thing to get a protein expressed in a plant in a laboratory; it's another thing altogether to get the trait expressed in a plant in the real world. Proponents of biotechnology have been talking about the remarkable promise of this technology for more than 20 years, but the only two commercially significant traits on the market today are herbicide tolerance and insect resistance. Part of the reason for the relatively few traits is that getting plants to do some of the things that developers long ago envisioned has proven to be more difficult than originally expected.

For example, Ingo Potrykus's development saga of "golden rice" continues today, years after the original concepts and early products were tested. Researchers are now following up on the recent development of SGR2, a golden rice variety developed by Syngenta that may produce ten times as much beta-carotene as the original SGR1 variety (Derham, 2005). Drought tolerance, a trait long pursued by plant-biotech developers in the private and non-profit sectors, appears at last to be close to moving toward the regulatory approval phase (Melcer, 2004). Even when gene sequences are successfully identified, it takes time to integrate that trait successfully into a variety with desirable agronomic or output traits. The science of plant genomics is moving ahead quite rapidly, but the complexity of gene modification to achieve commercially acceptable output or input traits is still a time-consuming and somewhat uncertain process.

One issue related to technical feasibility is access to intellectual property (IP). The impact of the introduction of strong IP-protection schemes in the plant-breeding and plant-biotech world remains a hotly debated issue. However, it seems fairly clear that, at a minimum, the development of strong IP-protection schemes raises the transaction costs (in time and money) for non-profit developers by requiring due-diligence searches to avoid infringement and to negotiate licensing arrangements when needed. On the other hand, strong IP protection is a precondition to investment by the private sector (Alston, 2004; BIO, 2005b).

Proving technical feasibility clearly remains a challenge for a number of specific non-food health and environmental plant-biotech applications. For pharmaceutical crops, for example, it remains to be seen whether plants can be modified and grown in a manner that allows consistent expression of the protein, and whether the protein will prove to be clinically equivalent and equally safe and effective as those grown in animal-cell cultures. Merispase®, a PMP designed to treat a condition that affects patients with cystic fibrosis, has been through some phase-II clinical trials intended to answer these types of questions (Meristem, 2005). Whether the predicted cost efficiencies will be realized is another key issue associated with proof of concept for PMPs.

Biotechnology applications to forestry are complicated by limited scientific knowledge of tree genomics as well as the inherent complexity of engineering an organism intended to grow for years before harvesting (PIFB, 2001). For example, it is possible that genetic changes could result in undesirable effects that would not be observed until after several years growth. Ensuring consistent expression of traits over the lifetime of a tree is also important for traits like insect and disease resistance (PIFB, 2001).

In the area of phytoremediation, there are promising laboratory and field-trial developments using genetic modifications to enhance plants' abilities to take up environmental contaminants such as metals (Bañuelos *et al.*, 2005). The question, of course, is how well such plants will work in the real world of contaminated sites; to date, field-trial data have been limited to simulated contaminated sites. For reasons discussed later in this paper, more compelling data of the efficacy and efficiency of this technology are likely to be needed before it will be applied in real-world environmental clean ups.

Product Management and Stewardship

The second hurdle is the cost of management and stewardship associated particularly with the development of bioengineered plants. Because of the environmental, food-safety, and marketing issues associated with bioengineered plants, they require special handling and management to ensure containment and, in some cases, tracking and identity preservation. Management and stewardship requirements start early in the development process, long before a plant may be ready to be commercialized; indeed, key product-development phases, including field trials, will be required to be under US Department of Agriculture (USDA) permit.

Arguably, these stewardship and management costs could be considered a part of regulatory compliance costs, because in many cases these requirements are actually mandated by regulatory agencies—as with USDA transportation and field-trial permits or notifications. On the other hand, it could also be argued that bioengineered crops would be subject to special handling and management even in the absence of regulatory requirements given potential concerns about liability under the common law of torts (Kershen, 2002) or to fulfill private contractual requirements. Particularly in the wake of the StarLink™ episode, seed companies, farmers, grain distributors and processors, and others in the food-production chain have become more conscious of the need to adopt best management practices to ensure that customers are getting what has been represented, and to avoid potential liability for GM-plant products mixing with plants where GM components are undesirable for any number of reasons.

However, as a representative of ProdiGene (2004) noted in a recent comment to USDA:

> *…no matter what system of production is employed, accidents, natural disasters, or other unforeseen events may allow the loss of containment despite best efforts.... [D]espite adherence to rigorous containment protocols, low level products not intended for food or feed have the potential to be present in commercial crops at some time.*

Given this potential, developers and investors seeking to reduce potential exposure to risk are likely to consider the availability of liability insurance in this area.

Part of the difficulty faced by developers and investors in this area is the lack of clarity and certainty about the standards to which they are being held accountable. At the present time, there are no legally binding standards or even guidelines to provide developers a "clear harbor" for adventitious presence. In the absence of legislation or regulation, liability will be determined through the rather ineffective process of litigation. To date, few cases have been litigated that shed any light on appropriate duties and responsibilities, leaving the field ripe for speculation by lawyers in law-review articles (Kershen, 2002).

Not even the regulatory agencies have taken on the task of defining tolerances or thresholds for materials from GM plants that have not completed the regulatory review process. Instead, USDA and EPA have imposed conditions on field trials that are, as a practical matter, intended to prevent any gene flow and thereby achieve a zero-tolerance level (PIFB, 2004b). Not only are these conditions expensive to follow, their existence implies there may be a legal liability for even a *de-minimus* level of contamination. It is also unclear if these conditions will be successful 100% of the time.

This issue has already been a particular challenge for developers of PMPs. Farmers, food manufacturers and others have expressed concern about any mixing of PMPs with food or feed crops, even if such mixing is unlikely to raise any environmental or health concern (Nutraceuticals International, 2003). Clearly, food manufacturers are concerned about the potential economic damage to their brands in the event of a publicized event where PMPs are found in their products. Growers are concerned that even the remote possibility of adventitious presence of PMPs in their food or feed crops could dry up lucrative markets, particularly in nations with markets hostile toward GM crops. This concern recently became a reality when Ventria's proposal to grow rice that has been genetically modified to produce a pharmaceutical compound in Missouri prompted Anheuser-Busch and Riceland Foods to threaten to boycott all rice produced in Missouri (Kasler, 2005).

Stewardship and management issues may also pose a challenge to the developers of GM-forestry applications, particularly given the long lifetimes of plantation trees. While somewhat different, given the food application, there have already been two incidents over gene flow from GM papaya trees to conventional papaya trees in Hawaii and Thailand (Creamer, 2004; Elias, 2004; Mathes, 2005). As the technology moves forward, there almost certainly will be issues associated with managing gene flow from GM trees in plantations to trees in unmanaged forests.

Managing plants to prevent unintended gene flow is less likely to be a concern with GM plants intended for phytoremediation since such plants are intended to be used on contaminated sites, far from any food or feed crops. How these plants are disposed of, however, will need to be the subject of careful consideration so that further soil contamination does not take place and to ensure these plants do not inadvertently move into the food or feed chain.

Management and stewardship issues are particularly troubling for university and other non-profit researchers who generally lack the experience of navigating regulatory requirements and managing long-term field trials under conditions of strict confinement.

Moreover, university researchers frequently lack the infrastructure and funding for such activities, an issue discussed in more detail below.

Management and stewardship requirements have clearly emerged as a significant hurdle—in money, resources, and time—on the road to product commercialization or deployment. What has made it even more difficult, of course, for developers and investors trying to make judgments about development costs, is that there remain significant uncertainties about the standards to which developers are expected to adhere. Clearly, the development of gene-expression restriction technologies, like those described by Roger Beachy elsewhere in this volume, would go a long way to reducing the costs of managing unwanted gene flow.

Regulatory Requirements—Direct Costs

The third major "speed bump" in the road to product commercialization is the regulatory review and approval process. Regulations impose additional costs on the development of bioengineered plants compared to improved varieties created through conventional breeding, but it is difficult to estimate the cost with any great precision (Alston and Kalaitzandonakes, 2005). Certainly much of the product-testing and development work required by regulators would be conducted by developers in any case, simply as a part of ensuring the quality, safety and performance of a new GM plant. As noted above, management and stewardship costs would, in many cases, be required by prudent business practices even in the absence of regulation. But, plainly, the costs associated with additional testing, data production, data-package submission, and the time associated with regulatory review, are significant. Costs for some of the initial GM-crop approvals have been estimated at $5 million to $15 million (Alston, 2004). Some analysts have estimated that half of all total development costs are associated with regulatory requirements (PIFB, 2004a). However, these costs have not been well characterized and studies are ongoing to obtain some independent analysis of those estimates.

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One of the factors affecting the costs of regulatory approval is the novelty of the trait or the novelty of the product in which the trait is being inserted. Not surprisingly, regulators tend to approach novel issues with greater caution, often demanding more studies and additional information to help answer their questions. As a result, first products through the regulatory system unquestionably bear a disproportionate amount of the regulatory burden. Today, it is unlikely that approval of a commodity food crop with a genetic construct already approved by the regulatory agencies would cost as much or take as long as the initial approval. On the other hand, a recent report by the Center for Science in the Public Interest noted that the time for regulatory approval of a new GM plant appears to be growing longer, not shorter, even though the plants being reviewed did not seem to present novel regulatory issues (Jaffe, 2005, this volume).

Once again, the regulatory approval hurdle places a disproportionate burden on university and other non-profit researchers who lack the experience with navigating the regulatory agencies and, perhaps more importantly, often lack the funding to carry out the required testing and to prepare the regulatory approval documents. Most non-profit researchers rely on government or foundation grants that typically support basic research, but not the kind of "regulatory science" needed to develop the data package to obtain product approvals (PIFB, 2004a).

Regulatory Requirements—Indirect Costs

The most visible cost of regulation is the direct cost of testing, data submission, and delay. Delaying the time in which the product can come to market imposes real costs, particularly for products that have time-limited intellectual property protection.

Beyond these direct costs is another, perhaps less obvious set of costs associated with regulatory uncertainty. In this case, the issue is not so much about what the regulations currently require, but uncertainty about what the regulations might require in the future. Without clarity from an agency about what a product approval requires, it is impossible for developers and potential investors to estimate the total costs of bringing a product to market. Today, for example, a developer may have a fairly good sense of what it would cost to bring another *Bt* or herbicide-tolerance gene through the regulatory system. But the question of what it will cost to approve a different type of trait—such as a drought-resistance gene—is much less certain. That kind of uncertainty discourages private-sector investment.

While some parts of the regulatory framework are relatively clear, others are not. As noted previously, agencies have not addressed the issue of adventitious presence except through permit requirements intended to prevent it from occurring. Even here, the rules continue to shift, as occurred in 2003 when USDA increased setback requirements and other conditions on PMP permits, sharply limiting where PMP field trials could be conducted. The White House Office of Science and Technology Policy has called on EPA, FDA and USDA to adopt rules to address adventitious presence resulting from field trials of GM crops intended for use as food or feed (OSTP, 2002), but there has been no similar call for guidance on plants not intended for use as food or feed—such as PMPs. While USDA has indicated that PMPs will always remain under APHIS permit, the Food and Drug Administration (FDA) could also exercise its authority over the drug-manufacturing process to oversee the planting, growing, harvesting, and transporting of PMPs (FDA, 2002).

New products inevitably raise novel issues for regulators. For example, it is not clear how plants modified through biotechnology for phytoremediation purposes will be regulated. While USDA's rules with respect to transport and field testing would certainly appear to apply, EPA has asserted that it has the authority—not exercised to date—to regulate plants intended for commercial bioremediation under the Toxic Substances Control Act as "new chemical substances" (EPA, 2005).

Likewise, while USDA's authority over GM trees is fairly clear, whether USDA will "deregulate" long-lived trees intended for plantations—or what information it would

require to make that decision—is much less clear. (EPA would presumably be in charge of approving pest-resistant trees under the pesticide laws.) Even more opaque is how USDA would make a decision to approve the release of a GM disease-resistant chestnut intended to grow and spread in unmanaged forests.

It's worth noting here that the regulatory system for GM plants is a paragon of clarity compared to the regulatory system for transgenic animals, where we still lack any formal statement from the administration as to what agency is responsible for what decisions about transgenic animals.

Finally, the ever-changing international regulatory environment poses an additional set of challenges for plant products that move out of the United States. In addition to specific laws adopted by countries with respect to GM foods and GM crops, the Cartagena Protocol on Biosafety continues to evolve and will certainly affect the inter-boundary transportation of any type of genetically modified organism, including plants and trees. How the Cartagena Protocol will continue to evolve and whether it will impose new legal or regulatory requirements remain a major source of uncertainty.

Marketplace Acceptance

The final hurdle is, of course, the test of the marketplace. As with any new product, the question will be whether buyers are willing to pay a price for it that returns a profit to its developers.

Are there any unique marketplace challenges that face health and environmental applications of plant biotechnology? The history of the introduction of GM foods offers a cautionary tale. Regardless of regulatory approvals, consumers in a number of countries remain suspicious about, and hostile to, GM crops and foods. In a market where consumers have alternative choices, their rejection of GM foods has had an enormous impact on trade and has dramatically slowed the introduction of new varieties of GM foods. Farmers, food manufacturers, grain processors and distributors and others have balked at the introduction of new GM varieties out of concern over negative consumer and marketplace reaction. GM potatoes, GM wheat, and GM sugar beets are all examples of products that made it through the regulatory process, but were rejected in the marketplace.

There are a number of reasons to believe that consumer and market attitudes toward non-food products of plant biotechnology may be different.

First, there is some reason to believe that the opposition to biotechnology is tied to its use as food. While there are environmental and other concerns about GM plants in Europe, the strongest opposition is associated with GM food products, and the opposition is based in large part on fears about safety (Allum *et al.*, 2003). In comparison, there has been little opposition to the non-food products of GM plants, such as cotton. For example, there has been little consumer opposition to blue jeans and few demands that they be labeled. So there is some reason to believe that the stigma attached to food biotechnology in some parts of the world may not automatically translate to other non-food applications of plant biotechnology.

Second, since the public is the ultimate buyer and consumer of GM foods, its choices have enormous influence on the food-marketing chain. Farmers may be enthusiastic

buyers of GM seeds, but unless they can find markets for their crops, they will buy something else. Interestingly, consumers appear to be most concerned about foods that contain GM ingredients but there is far less concern about meat or milk from animals fed with GM grains.

In most of the non-food health and environmental applications of biotechnology, however, the public is not the buyer, and the products and services they ultimately receive are not "genetically modified." For example, the buyers of lumber and pulp are simply businesses that, like farmers, are concerned primarily with cost and performance. The forestry products ultimately bought by consumers—paper, cardboard, houses—do not contain "GMOs."

Similarly, the "product" bought and used by consumers from GM plants that produce PMPs is the drug or therapeutic protein itself—typically prescribed by a doctor and approved by the FDA. Again, the product will be long divorced from the process by which it was made.

Third, at least some of the consumer opposition to GM food has been the result of a risk-benefit consideration where consumers see no benefit in the current generation of GM foods and elevated risk. Health and environmental plant-biotechnology applications, almost by definition, offer the prospects either for public benefits or direct consumer benefits. Using plants to produce lower-cost, potentially safer drugs has the strong support of a number of disease-research advocacy groups.

The fact is, consumers do make distinctions among applications of plant biotechnology (PIFB, 2005). It should not be surprising, for instance, that in light of the above discussion, the applications of plant biotechnology most strongly supported by Americans are those that would provide lower-cost pharmaceuticals or that would reduce world hunger (Figure 1).

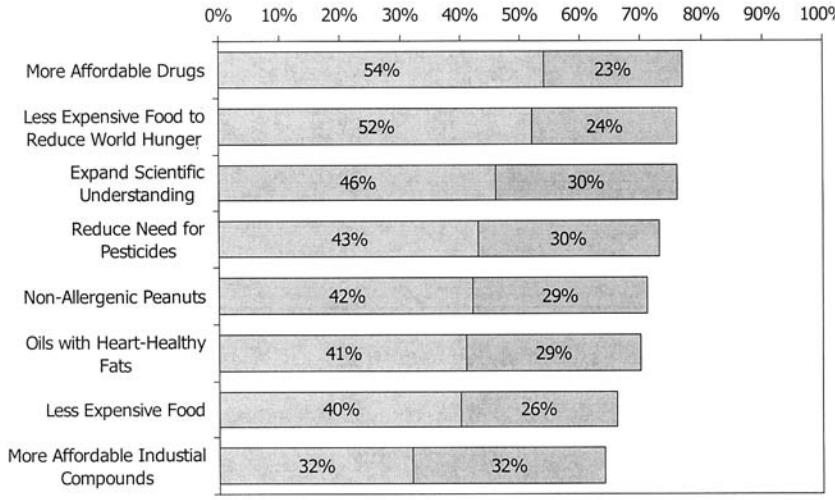

Figure 1. Ratings of "very good" or "somewhat good" reasons, respectively, to produce GM plants (PIFB, 2005).

Nevertheless, given the history of predictions about biotechnology, one must be humble when predicting the future. It frankly is too early to know whether the stigma against GM technology in some parts of the world will cling to these health and environmental applications. Mixed in with concerns about food safety are environmental concerns and embedded cultural, social, and economic issues that are often not clearly expressed. Even in the absence of a food-safety issue and direct consumer concerns, some of these other issues could still surface as opposition that could impact the market acceptability of these products.

In particular, the use of biotechnology in forestry will almost certainly be controversial, if for no other reason than, as with aquaculture and agriculture, there already are strong disagreements about the role of intensive forestry practices. To the extent that biotechnology makes plantation forests more economically viable, it is likely that it will be opposed by those who are already critical of existing forestry practices. In addition, forests have a cultural significance that row crops do not. In a PIFB-sponsored conference in 2001, a number of speakers referred to the emotional and moral value that people place on forests as natural places worthy of protection and respect. As a consequence, people are more likely to view the use of genetic modification technologies in forestry as unnatural, which could conceivably translate into opposition to forest products derived from GM trees along the lines of similar campaigns relating to "sustainable" forestry (PIFB, 2001).

On the other hand, potential environmental benefits from this technology may be appealing to some of the same segment of the public. For example, the ability to grow trees that require less energy to produce paper and pulp could be seen as an environmental benefit, not to mention the development of disease-resistant varieties of elm, chestnut, and dogwood. And the ability to create disease-resistant strains of key tree species could introduce the unique ability to preserve species that otherwise might become extinct. As noted, concerns about PMPs have little to do with the products, but rather with the potential that gene flow could move unwanted biological materials into food or feed crops.

GM plants intended for use in environmental clean ups present a different set of marketing issues, since the primary buyer is the government or a clean up contractor working under government standards. As with any treatment technology, regulators choosing a particular remediation technology must find the product to be "protective of human health and environment, maintain protection over time, and minimize untreated waste" (40 CFR 300. 430). For example, if a treatment technology is being selected for use in the clean up of a Superfund site, the EPA remedial project manager is required to consider nine factors to evaluate alternatives and determine the remedy preference, with cost being merely one of the considerations (EPA, 1990).

The environmental-technology market is highly risk-adverse (OTA, 1985). Government and their contractors do not want to take a chance in adopting a technology that does not work and risks making a problem worse. EPA has noted that clean up-project managers will need strong assurances—and a viable backup plan in the event of failure—before they are likely to select phytoremediation as an option (EPA, 2005). Community support is an additional factor in remediation-technology choices. If there is concern about the use of GM plants, public opposition could constrain the use of this particular technology.

On the other hand, communities could embrace GM phytoremediation as a cost-effective, quick, and more "natural" process than employing chemical or thermal destruction treatment processes, or more desirable than typical dig-and-dump techniques. It simply is too early, particularly without experience using GM phytoremediation in real-world clean up tests, to know what the public will accept.

Conclusion

The hurdles to commercialization of health and environmental plant-biotechnology applications are significant. Much about them is uncertain. Few developers have the kind of financial security or "bet the company" attitude to risk being the first product to "test" the system. Unquestionably, some potentially valuable applications remain sitting on bench shelves in universities and companies around the country waiting for someone else to go first.

Few developers have the kind of financial security or "bet the company" attitude to risk being the first product to "test" the system.

Nevertheless, there are reasons for cautious optimism. The regulatory system is slowly responding to the need to evolve for new and different types of biotechnology products. Management and stewardship requirements are becoming more clear. And experience suggests that the market welcomes safe, innovative products that provide perceived benefits to buyers and to the public. The marketplace makes distinctions between products—even between products made with biotechnology.

Not surprisingly, Pew Initiative polls tend to show that when consumers see a strong benefit for themselves, their families, or their community, they respond positively. As this technology moves forward, the bulk of the concern and opposition may prove to be rooted in food and the unwillingness of affluent consumers to take a small perceived risk in the absence of a clear benefit. The challenge then to the developers is to ensure that the potential benefits of this technology are clearly explained to the public while the government continues to ensure safety. If developers can do that, then there is indeed a way to "get there from here."

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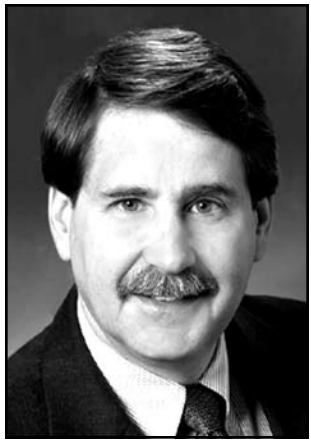

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