
Biotechnology: Catalyst for Change in Agriculture

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The modern agricultural industry has been highly effective in the implementation of productive new technologies that provide more food, shelter, and industrial materials for an expanding world population. Agricultural output needed to produce an abundant food supply for nations where economies and distribution systems are adequate is currently achieved on approximately six million square miles of cultivated land, the same land use as in 1950, despite a doubling in world population throughout this period. Such expanding productivity, on constant or even diminishing agricultural land, is an essential component of the sustainable agricultural system we all hope to develop. It can only be achieved through continued scientific discovery to improve germplasm and production practices throughout the world. There is no greater opportunity today to accomplish this than through the application of biotechnology.

Increased global information exchange, international trade, and rapid innovation in many areas of technology — especially biotechnology — are now contributing to an evolution in the world agricultural industry, through which substantial enhancement in our industry will occur much faster than ever before. We will see more rapid improvement and global distribution of germplasm and production practices, and we must prepare to deal with entirely novel applications for agricultural land use. More so than any previous agricultural technology infusion, biotechnology will impact all elements of the industry, all associated industries, and all of interfacing society. The increased speed and the extreme breadth of current change make this a particularly unsettling time. Now, as never before, there is need for industry, academia, and consumer interests to cooperate in the identification and management of issues generated by this new technology. We must deal with new laws and regulations, new products and industry practices, and entirely new agricultural uses that will emerge as the potential of biotechnology is realized.

Two circumstances are important in considering the magnitude of the situation we now face. First is the exceptional power of biotechnology to enable rapid and precise manipulation of plant and animal genetics in ways that were never previously feasible. Second, the application of biotechnology to other industries beyond agriculture ensures that a massive level of research and development expenditure will continue to fuel improvement in biotechnical skills for the foreseeable future. Available resources for continued research and technology development will be well above the historically low levels of funding that have been targeted solely toward agriculture, and advances in other industries will significantly contribute toward the rate of progress in our own industry.

In this presentation I will discuss the breadth of the enabling technology, its management through the intellectual property system, and the effects we should anticipate as our industry adjusts to a more rapid pace in new product development.

THE TECHNOLOGY

Biotechnology enables the precise alteration of metabolic processes of living organisms to achieve novel outcomes. Advances in this field have relied upon broad innovation in our understanding and manipulation of living materials, which is achieved through the sciences of molecular and cellular biology. Molecular biology is the study and manipulation of DNA, which is the common “blueprint” of all living organisms. Such strong similarities exist in the character of DNA from all life forms that a common technology base is broadly applicable toward gene discovery, gene mapping and tracking, and even the genetic engineering of diverse microbial, plant, and animal systems. Cell biology, also an integral aspect of biotechnology, is essentially the study of structure and function of living cells. Like molecular biology, many principles of cell biology can be generalized across species.

The necessary laboratory equipment and intellectual skills needed for research in molecular and cellular biology have evolved dramatically over the past two decades, and essential capabilities are already in place in most of the world’s major academic and industrial centers worldwide, including not only those which focus solely on agriculture, but other industries as well. Because of the common interest in the application of molecular and cellular biology to the health care, chemical, and other high-value industries, research and development advances toward agricultural objectives will be furthered by discoveries from outside our field. For example, molecular breeding technology, now widely used to facilitate new crop development, continues to benefit greatly from human genome mapping efforts. In addition, the refinement of gene mapping technology will contribute to our increased understanding of the existing mechanisms by which plants and animals adapt to, and deal with, their envi-

ronments, leading to new opportunities to engineer crop improvements in years ahead. However, it is the transfer of genetic information from one organism to another, even across species boundaries, that represents the most powerful new opportunity for the improvement of plants and animals.

Many schemes have been developed for gene transfer to live organisms and much of the technology is applicable toward any living cell, regardless of species. While plant sciences have often followed the advancement of other industries due to greater financial resources being directed toward fields such as health care, the engineering of plants has progressed considerably faster than comparable efforts in animals or humans because of practical and social considerations. Gene delivery to all major plant species has already been achieved, and the rate of continuing progress in refining crop gene delivery technology is dramatic. With such powerful enabling technology in hand, our industry is now turning to issues of new product development.

EVOLUTION OF THE AGRICULTURAL INDUSTRY

We are currently in the midst of an evolution in agriculture, provoked by the maturation of biotechnology from the stage of concept development to application. It is practical to view this evolution in three phases, each spanning approximately a decade. The process began in earnest with a period of concept evaluation and enabling technology development during the 1980s. This was followed by a transition from technology development to early product development, which is now underway. The evolution will continue, following the turn of the next century, with more extensive product development, which will lead to new agricultural applications and dramatic industry expansion.

The 1980s was an extraordinary period of technology enablement during which biotechnical methods were generated for gene identification, gene cloning and characterization, and for the delivery of genes to plants and animals. Hundreds of millions of new dollars were infused into agricultural research — much of it from the private sector — without any immediate financial return through sale of products. It was indeed fortunate for our progress in this emerging field that private sector funding was available, since the early technology development was very costly and occurred as federal research support began to decline. With many of the new technologies now on line, the industry is increasing its focus on product-oriented research, while continuing to refine essential aspects of enabling technology for the future. Although marketable products were not generated during the 1980s, a significant outcome from that period of discovery was intellectual property. The past decade was not unlike the land rush of the past century, and many claims were staked — large and small — that will shape the development of the industry through the ongoing transition.

The agricultural industry in the 1990s will be dominated by a transition from biotechnology development toward product and market development. We are now in the midst of this change, with the first of the new products reaching the marketplace in launches of unprecedented scope. Insect resistant cotton and corn, herbicide resistant crops, and other early products have all been released to a very receptive marketplace. Continued product success will ultimately depend on the level of consistent value delivered to the consumer, but all current indications show that new and faster product development will be a major benefit to our industry. Years of research and product testing have gone into each of the products now reaching the market, and the first revenues from actual product sales are being welcomed by industry investors. However, the development of those new products has further revealed peripheral industry issues that result from the use of biotechnology. The creative revision of market paradigms to enable sufficient value capture from novel products must now be undertaken.

Following the turn of the century, the third decade of this evolution will be characterized by more complex product development and significant commercial expansion. We will watch value shift away from classical agricultural chemical inputs toward more versatile crop and animal genetics. Industry consolidation will continue through alliances and acquisitions, and the trend toward vertical integration will escalate to enable more effective product management and value capture. Many of the small companies that pursued technology development in the past will have insufficient resources to move products to market in a timely way, and many will close or be acquired by larger firms. Companies of greater size and resources will adapt to the changing environment, new production and marketing strategies will be established, and entirely new business areas will be opened to exploit agricultural technology. Among the key elements shaping these industry adaptations to the new technology will be ownership and control of new technologies and resulting products. While various commercial practices will contribute to such control, there will be a strong influence from the patent system.

INTELLECTUAL PROPERTY IN AGRICULTURE

The generation of biotechnology skill has been very costly, and the application of the new technology will entail higher costs in shorter research and development cycles than historically practiced in agriculture. Government and foundation support to finance this technology over the past decade has been very limited. Increasing budget pressures in the federal government will make basic and discovery research dollars increasingly scarce. The situation is ironic: time frames in the enhancement of agricultural productivity are long, which is a detraction to industry, but benefits are seen across society. Government expenditures toward the enhancement of agricultural productivity have also historically provided an exceptionally strong societal return. However, we are

facing a period where the continued development of agricultural productivity will fall increasingly on private industry. For effective implementation of biotechnology, product value must be more reliably captured to reimburse even early stage researchers, or the product development pipeline will be diminished. As has been demonstrated in all other technology-dependent industries, patent law provides a mechanism to capture value when products are delivered to consumers. That value is then distributed to contributors along the development path.

A “patent” is a legal provision that provides an exclusive right to inventors for a limited period of time to “make, use, or sell” their discovery in return for releasing the knowledge of their invention to the general public. The patent system has served many other industries well in stimulating research, encouraging product development, and enabling the controlled distribution of products to consumers. Patents are neither new or untested in agriculture, yet their increased application to agricultural products must receive a much greater emphasis in years ahead. Acceptance of a stronger intellectual property system in agriculture has been slow.

Plant “certificate” protection was first offered with the Plant Patent Act (PPA) of 1930, when breeders were given the opportunity to protect asexually propagated crops developed through their breeding programs. Certificate protection was further extended in 1970 with the Plant Variety Protection Act (PVPA), which covered sexually propagated crops. However, an intriguing exclusion of a small class of crops — known as the “soup vegetables,” which included okra, carrots, celery, tomatoes, peppers, and cucumbers — provides a useful lesson for our current transition. The soup vegetable exclusion from the PVPA resulted from a concerted lobbying effort by an industry sector that feared proprietary protection would inhibit research and lead to increased vegetable costs. In practice over the following decade, however, the protected crops were the subject of increased research and development, with resulting yield and quality enhancement without unacceptable price increases. In 1980, an amendment to the PVPA was passed in which certificate protection was extended to cover the previously excluded soup vegetables. The lesson learned through a decade of practical experience was one that had already been learned in other industries: effective proprietary protection serves both the agricultural industry and consumers by enabling equitable value distribution for product innovations.

Proprietary protection for crops and animals was further extended when it was determined that utility patent law, which is distinct from the PVPA, can be applied to living organisms. Utility patents address products or processes that are novel, non-obvious, have a defined utility, and are clearly described to the general public, rather than maintained as trade secrets. The extension of utility patent law to engineered plants and animals came about through two landmark court rulings. In *Chakrabarty v. Diamond* (1980) it was determined that specific

claims covering engineered oil-degrading bacteria were allowable under utility patent law, because significant human intervention was required to generate the product. This case first clarified that newly created living materials were to be considered patentable products under utility patent law. The relevance to agriculture was further extended in a second case, *ex parte Hibberd* (1985), where it was determined that corn varieties with enhanced amino acid profiles were patentable under utility patent law in addition to what PVPA protection otherwise afforded. The effect of those two rulings was a dramatic escalation of patent filings addressing all aspects of biotechnology. The applications cover many now routine processes such as the use of DNA markers to streamline breeding programs, technologies to make and transfer genes, and the resulting engineered plants, seeds, and transgenic animal products from biotechnology.

Many early biotechnology patents have been issued, but still more remain under prosecution. Concerns have been raised by various parties over the number of new patents and the nature of claims that have emerged, based on fears that agricultural biotechnology patents might impede research and delay future product development. The current concerns are not unlike those which led to the soup vegetable exclusion from the PVPA of 1970. Once again, we can expect to find those fears to be unfounded. Research is proceeding in both academia and industry at a rapid pace, and there has been no effort from industry to extract value from research licenses to academia for the new technology. Indeed, many of the dominant patents in biotechnology are controlled by academic institutions, and license revenues are contributing support for academic research programs. Industry is effectively adjusting to the requirement for patent licenses, and launches of valuable new products have been initiated without inappropriate deterrence from licensing or litigation. The global management of patents is far more unsettled, and it will be many years before consistency emerges, particularly in nations that have not historically protected intellectual property.

The experience from other technology arenas is being followed in biotechnology — early patents addressed broad enabling concepts; later inventions are considerably more limited in scope. This is due to the requirement for novelty in inventions, and as technologies mature it becomes more difficult to achieve substantial advances that previously have not been disclosed to the public. The outcome of this maturation process is that broad patents influence industry development in the early years, while the more limited patents sustain long-term product advancement of the industry. What is unusual in agricultural biotechnology is that many of the most powerful patent applications, filed early in the last decade, still remain under prosecution due to lengthy delays imposed by prosecution backlogs and patent interference proceedings. These dominating patents will have strong influence on the shaping of our industry over the next two decades.

CAPTURING VALUE FROM BIOTECHNOLOGY

Genetic engineering of plants and animals is now well underway, with the essential technology components in hand to develop real products. Gene design and delivery technologies continue to be refined, useful genes for agronomic and production traits are being unveiled in increasing numbers, and product development is now the primary goal of our industry. However, the emergence of the first new products presents a series of complex issues to the industry regarding marketing and value capture.

The agricultural industry has historically been comprised of distinct segments including seed providers, growers, processors, distributors, and consumer outlets. We have generally relied on the passage of commodity materials from the farm, through processors, and on to consumers in distinct steps that capture increasing incremental value as the refined agricultural materials approach the end-user. A modern trend toward larger farming operations and vertical integration, combining processing and distribution, has been driven to date by economies of scale and other efficiencies provided by channeled flow of materials through a controlled development pathway. However, as biotechnology adds increasing value directly to germplasm, it will catalyze a series of changes in industry value-capture paradigms, which will lead to a more comprehensive transition toward identity preservation of crops from seed to consumer.

For agriculture to be successful, products and services must have both a tangible value and a mechanism to capture and return that value to product and service providers. It is common to exchange value at the farm gate through sale of germplasm and chemicals to growers at the processor level, where growers receive compensation for their agricultural produce in return for deliverables to the processor, and at the level of end-users, where processors and distributors receive monetary value from consumers. Biotechnology is now promoting the shift of a substantial component of crop value directly into the germplasm, but this comes at a substantial development expense. Herbicide resistance, pest and pathogen resistance, and various other traits of value to growers, processors, or consumers are already entering the marketplace in the form of new germplasm. These first product examples each involve genes encoding relatively simple, single-gene traits. The traits now being delivered are conceptually consistent with traits which have current market value. However, new mechanisms must be devised to allow payment to be equitably captured and diverted from growers, processors, distributors, and consumers to compensate developers of the novel germplasm.

Herbicide-resistant crops should enable growers to use more effective, ecologically sound and economical herbicides than are currently at their disposal. However, for such products to be effective in the marketplace, the

grower must receive a tangible advantage through enhanced productivity and decreased chemical expenditures. It is then reasonable to expect that a portion of the financial savings seen by the grower would be shared with the provider of the novel germplasm. This issue takes on still greater significance when insect-resistant crops are considered. Herbicide resistance shifts farm input expenditures from one chemical product to another, but insect resistance very substantially reduces overall expenditures for purchased chemicals and thereby generates much higher potential savings to the grower. The sharing of this savings with germplasm developers can be accomplished through either payment of a premium on seed sales, or as a direct licensing payment to the developer of the novel trait. However, such equitable value sharing is inconsistent with past industry practices that permit growers to save their own seed for planting in subsequent years, a practice that would naturally limit compensation delivered to those who initially created the novel germplasm. There are now legal restrictions against the reuse of saved seed where the materials are covered by utility patent claims, but industry acceptance must still be achieved. If such compensation cannot be reliably returned to germplasm developers, new cost-saving products will less likely become available to growers in the years ahead.

FASTER PRODUCT DEVELOPMENT

Biotechnology will contribute to the streamlining of product development cycles, or “cycle time,” in an industry where advancement has been generally slow and methodical. Plant and animal traits, which in the past were objectives of classical breeding programs, are already being generated in considerably shorter time frames through the use of gene mapping and tracking. Where formerly it may have been necessary to visually observe phenotypic traits in populations of progeny following genetic crosses, it is becoming routine to employ linked DNA markers to screen large numbers of progeny at an early stage of development — even in seed prior to planting — thereby limiting grow out to only the desired progeny. Analysis of the content of donor genome, relative to the recipient, and selection of the most advanced progeny, enables a more rapid introgression in far fewer breeding cycles. Thus, the rate of progress in development of new germplasm has already accelerated, and commercial products will become outdated more rapidly as replacements reach the market in shorter time frames. The shortened product-life will necessitate more effective value-capture mechanisms than in the past.

The physical transfer of genes encoding new traits provides a very powerful tool to further shorten the product development cycle. For example, in programs at Agracetus we have refined “gene gun” DNA delivery technology to achieve delivery of genes directly into seed of commercial crop varieties. This

enables the direct germination of transgenic plants without the need for tissue culture, thereby avoiding a process that both delays initial plant development and limits gene transfer to only those varieties which can be managed in culture. Our first transgenic plants, in elite commercial varieties, reach maturity within five months of project initiation and do not require time-consuming back crossing. Because genes encoding new and desirable traits can readily be moved across species boundaries, exceptionally diverse crop characteristics can now be generated in a single growing season.

There are many potential advantages of such rapid product development, but industry adaptation necessary to successfully manage these new capabilities will be complex. This is exemplified in a second example, in which Agracetus scientists have undertaken gene transfer programs to genetically engineer a stronger cotton fiber, a trait that has historically been subject to premium pricing and has been a long-term breeding target. The advantages of increased fiber strength are found at various levels of the fiber industry, from processing steps to consumer satisfaction. Stronger fiber is able to undergo more rapid processing without breakage as the thread, yarn, and cloth are mechanically constructed, and the faster product through-put enabled by stronger fiber converts to immediate savings on expensive capital equipment. In later processing steps, where the chemical and mechanical processes used to “finish” fabrics weaken fiber, a stronger fiber helps retain the durability characteristics that are valued by consumers.

Through classical breeding, the average strength of cotton fiber across the industry has been increasing at a relatively constant rate of 1.5 percent per year, with a cumulative strength increase of 16 percent achieved from 1980 to 1991. However, we are now able to use genetic engineering to dramatically increase the strength of cotton fiber with the addition of genes from other organisms. In our recent research project, the strength of the major upland cotton variety was increased by more than 60 percent with a single transferred gene. This represents a strength enhancement equivalent to 30 years of classical plant breeding in a fraction of that time, and the fiber strength achieved now exceeds the current premium system for fiber strength. Identity preservation of such specialty fibers or an altered premium structure will therefore be needed if exceptional value is to be captured. The industry has effectively adjusted to incremental improvements in many characteristics such as fiber strength and length, but must now consider the economic implications of more dramatic quality changes in shorter time frames. In the fiber industry, and in many other areas where crops are utilized, this will entail a more frequent evaluation of processing technology to efficiently take advantage of new inputs. The capital infrastructure for utilization of agriculture will need to become more flexible in order to accept radically new and varied materials enabled by biotechnology.

NEW PRODUCTS, NEW MARKETS

The ability to bring in new genes from different organisms further enables development of novel agricultural products, including products that will extend existing markets and those that will lead to entirely new business opportunities for agriculture. A second cotton fiber concept from *Agracetus* offers one example of a product that extends an existing agricultural product line. Our intent in this program is to improve, beyond the capacity of existing cotton germplasm, the dye-ability, chemical reactivity, absorbency, and structural dynamics of fiber (such as shrinkage and wrinkle resistance). Already developed through this program are fibers that contain polyester in the fiber core, and we have found that some of the more desirable characteristics of petroleum-based synthetic fibers are imparted to the “natural” cotton fiber. Similar programs to extend the current limits of materials derived from other crops are underway in many other laboratories where oil, starch, and protein alterations are being advanced beyond the capacity of existing germplasm. The revision of plant products in this manner, by bringing in genetic information from one organism to another, thus represents a broad opportunity to expand current plant product markets. However, such new products will require significant adjustment in processing practices and market structure to enable value capture from traits not routinely monitored by the industry today. Sale of transgenic seed to growers at a premium price will not be sufficient, even as proprietary protection becomes accepted, because the grower has no means to pass on costs downstream to processors. The outcome will be an additional push toward vertical integration, which will facilitate the channeling of identity-preserved products from the field to dedicated processors, and then on to the consumer.

The use of gene transfer between organisms also enables development of entirely new agricultural uses, such as the Plant Bioreactor Program of *Agracetus*. In this project, crops are used as production vessels to economically produce large quantities of new biological materials. It has long been recognized that plants provide the world’s most economical supply of proteins and complex secondary metabolites, but historically the diversity and concentrations of these materials were limited to what was found in nature or developed by man through classical plant breeding. Gene transfer now enables the engineering of crops to produce more of the valuable chemicals that are already found in some species, and also new materials currently derived from other sources. Targets of Plant Bioreactor Production include many high value biological products destined for industrial, food, feed, and even pharmaceutical application. Genetically engineered crops for each of those markets are currently in development in a number of laboratories worldwide, and early product candidates are already in field trials. Because the crops will require special handling in the field, dedicated processing, and delivery to specific end-users, vertical integration will clearly be a favored trend.

SUMMARY

Biotechnology represents a powerful new tool for plant and animal breeding, and the application of this technology will lead to new products and new uses for agriculture. This technology enables very rapid product development. The increased speed of accomplishing genetic improvements also condenses product development expense into much shorter time frames. These issues will necessitate changes in industry practice to ensure that appropriate value can be captured for the increased contribution of genetics as a component of final product value. Historically, high quality genetics have been critical to agricultural progress but have not fared well in capturing a significant portion of final product value. Paper packaging now captures greater value than the grain in a box of breakfast cereal. New paradigms for value capture will therefore evolve to more equitably distribute value from consumers to those participants earlier in the development path. The key industry changes to achieve this will be clarification and enforcement of a strong system for intellectual property protection, and vertical integration of the industry to coordinate value exchange from germplasm provider to consumer. While the most exciting aspect of biotechnology application to agriculture will be novel products and new uses for crops, even commodity agriculture will be affected by broad changes in industry management of crop value.