Chapter 10

U.S. Investment in Biotechnology Applied to Plant Agriculture

"Let us never forget that the cultivation of the earth is the most important labor of man."

—Daniel Webster
January 13, 1840

"... whoever could make two ears of corn, or two blades of grass, to grow upon a spot of ground where only one grew before, would deserve better of mankind, and do more essential service to his country, than the whole race of politicians put together."

–Swift
Gulliver's Travels: Voyage ***to Brobdingnag***

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Agricultura] research in the United States is not monolithic. It uses both traditional methods, such as plant and animal breeding, and newer biotechniques, such as genetic engineering. It spans a broad range of applications, extending from livestock to fisheries to crops to forests to microorganisms. U.S. agricultural research is a longstanding institution with public and private sector components. And, while it is often difficult to compartmentalize the diverse components of agricultural research, this chapter focuses on U.S. investment—both human and financial capital—in biotechnological research of plants in agriculture. Who invests in plant agricultural biotechnology research, and what factors influence the amount invested and how the funding is used? What actions are necessary to enhance the development of agricultural research?

An analysis of plant biotechnology research must include a discussion of the firmly established (and necessary) traditional technology component, i.e., plant breeding. Thus, while this chapter focuses on biotechnological applications, it examines, to a lesser extent, the delicate balance between research with the new techniques v. traditional agricultural research. Because it is difficult to separate research activity from commercial development in plant biotechnology, this chapter first examines factors influencing investment in U.S. plant agricultural research, and then briefly examines issues important to commercialization of such research.

This chapter principally examines investment in plant agricultural biotechnology and issues that affect the dollar flow (rather than, for example, the impact of biotechnology on farms or on the extension service). A comprehensive analysis of biotechnology and its impact on the infrastructure of American agriculture was assessed in the 1986 OTA report ***Technology, Public Policy, and the Changing Structure of American Agriculture (101). While micro-organisms*** play a pivotal role in plant biotechnology research and development (R&D), examining micro-organismal applications is beyond the scope of this chapter. Finally, although plant agricultural applications of biotechnology play a central role in discussions about environmental risks of biotechnology, these issues are addressed in a separate OTA report in this series (96).

FACTORS INFLUENCING U.S. INVESTMENT IN AGRICULTURAL RESEARCH

US. agriculture—plant and animal—is one of the most efficient and productive sectors in this country's economy. Despite declines in recent years, the U.S. agricultural trade balance has added a surplus to the U.S. trade account every year since 1960 (91, 101). Agriculture contributes to, directly or indirectly, approximately 20 percent of the gross national product, 23 percent of the nation's employment, and 19 percent of export earnings (77).

Increasingly, however, myriad problems beset U.S. agriculture. Complex in nature and scope, they include the declining competitive position of U.S. agricultural products in international markets, increasing commodity surpluses, low profitability for significant numbers of farmers, and environmental effects of agrichemicals (83,102). Research alone cannot solve these problems, but can contribute to their solution if resources, human and financial, are available (83)102). Thus, although the problems facing agriculture are **serious,** the **impact** of Federal R&Din this sector in particular can be powerful (100).

The benefits of agricultural research are substantial. The U.S. Department of Agriculture (USDA) claims the annual rate of return for investment in agricultural research is between 30 and 50 percent per year (83)104). Other estimates of rate of return vary from 21 percent to 110 percent, with the vast majority in the 33 to 66 percent range (100). In particular, biotechnology products are expected to improve international competitiveness of U.S. agricultural products (101).

Over the past decade and a half, however, the U.S. agricultural research system has undergone increased scrutiny and criticism (66,48)81). Agricultural research endeavors, including biotechnological applications, are presently in a state of flux. Several factors affect, or have affected, the investment forecast for agri-biotechnological research, including:

- the discovery of the new technologies themselves,
- intellectual property rights for plants,
- the funding source of plant agricultural biotechnology research,
- the regulatory environment,
- domestic political and economic conditions, and
- international markets.

With such a range of pressures, the emphasis in U.S. plant biotechnology constantly shifts to derive the optimum formula to achieve the maximum return possible. The following sections focus on how investment in plant agricultural research responded or is responding to the first three factors: the advent of the biotechniques; plant ownership; and private v. public plant research funding.

THE BIOTECHNIQUES IN AGRICULTURAL RESEARCH

New biotechnologies have the potential to modify plants so that they can resist insects and disease, grow in harsh environments, provide their own nitrogen fertilizer, or be more nutritious. Technical barriers, however, still exist. In particular, widespread success in applications for multigenic traits (such as salt tolerance or stress resistance) will for the present remain elusive (17,44), perhaps decades away (6,101). Nevertheless, the newer technologies can potentially lower costs and accelerate the rate, precision, reliability, and scope of improvements beyond that possible by traditional plant breeding (68,101).

Two broad classes of biotechniques--cell culture and recombinant DNA—are likely to have an impact on the production of new plant varieties. Plant tissue and cell culture date from the turn of the century, but were only minimally exploited until the late 1950s (6). Successful in vitro cultivation of plant cells and related culturing techniques underlie today’s gene transfer techniques and subsequent regeneration of altered, whole plants. Plant tissue and cell culture are also critical tools for increasing fundamental knowledge through basic research. The history of genetic engineering and a detailed description of the principles of recombinant DNA technology are discussed in an earlier OTA report in this series (97). In general, the fundamentals of genetic engineering are similar for microbial, animal, and plant applications, but developing some new approaches for plant systems has been necessary.

The endpoints of crop improvement using biotechnology are those of traditional breeding: increased yield, improved qualitative traits, and reduced labor and production costs. New products not previously associated with classical methods also appear possible. Box 10-A briefly describes some of the new biotechniques exploited to achieve these aims. Comprehensive descriptions of strategies designed to transfer foreign genes to plants and plant cells have been published elsewhere (19,21,57,67,68,70,88).

Applications of the Techniques

The new biotechniques are useful for investigating diverse problems and plant types. For example, plant tissue and cell culture is an important technique for breeders. It can be used for screening, at the cellular level, potentially useful traits. As many as ten million cell aggregates can be cultured in a single 250 ml flask (less than 1 cup). This can be compared to a space require-

Box 10-A.-Techniques Used in Plant Biotechnology

Plant Tissue and cell culture. Plant cultures can be started from single cells, or pieces of plant tissue. Cultures are grown on solid or in liquid media. Several species of plants, including alfalfa, blueberry, carrot, corn, rice, soybean, sunflower, tobacco, tomato, and wheat, can be cultured in vitro (3).

Plant Regeneration. Regenerating intact, viable organisms from single ceils, protoplasts, or tissue is unique to plants and pivotal to successful genetic engineering of crop species. (To produce a protoplast, scientists use enzymes to digest away the plant cell wall.) Although genes can be transferred and examined in laboratory cultures, ultimate success is achieved only if the culture can be regenerated and the characteristic expressed in the whole plant. Figure 10-1 illustrates steps involved in regenerating plants in vitro.

Protoplast Fusion. Protoplasts from different parent cells are artificially fused to form a single hybrid cell with the genetic material from each parent. Protoplasm fusions are useful for transferring multigenic traits or for fusing cells from plants that cannot be crossed sexually (68), thus permitting the exchange of genetic information beyond natural breeding barriers. Successful gene transfer via protoplasm fusion depends on the ability to regenerate a mature plant from the fusion product.

***Agrobacterium tumefaciens* plasmid** One of the most widely used and probably the best characterized system for transferring foreign genes into plant cells is Ti plasmid-mediated transfer (88). The technique involves a plasmid vector (Ti plasmid) isolated from ***Agrobacterium tumefaciens*, a** naturally occurring soil-borne bacteria that can introduce genetic information stably into certain plant cells in nature. Using recombinant DNA technology, the plasmid has been modified to increase its efficacy in the laboratory.

Transformation (Direct DNA Uptake). Certain chemical or electrical treatments allow direct uptake and incorporation of foreign DNA into plant protoplasts--a process called transformation. Since hundreds of thousands of cells can be simultaneously treated, transformation is a relatively easy technique. Cells expressing the desired trait can be regenerated and tested further.

Microinjection. Using a special apparatus, fine glass micropipettes, and a microscope, DNA is directly introduced into individual cells or cell nuclei (in plants, protoplasts are usually used). The process is more labor-intensive than transformation, requiring a trained worker. Although fewer cells can be injected with DNA than in mass transformation, a higher frequency of successful uptake and incorporation of the foreign genetic material can be achieved (68)–up to 14 percent of injected cells (22).

Virus-Mediated Transfer. Virus-mediated transfer of DNA has played a critical role in nonplant applications of biotechnology. But in large part due to an underdeveloped knowledge base, viral vectors for plant systems generally have not been exploited (68). Cauliflower mosaic virus has been used with some success in turnips (14,68),. and Brome mosaic virus in barley (35,68). Developing generic virus-mediated transfer systems could accelerate progress in plant biotechnology.

DNA Shotgun. One novel approach uses gunpowder to deliver DNA into plant cells (54). The DNA to be transferred is put onto the surface of four micrometer tungsten particles and propelled into a plant cell by a specially designed gun. Figure 10-2 is a photograph of an onion cell with such microprojectiles visible within its confines. While an innovative approach, it is unclear whether it will prove to be a routine method for gene transfer in monocots (15).

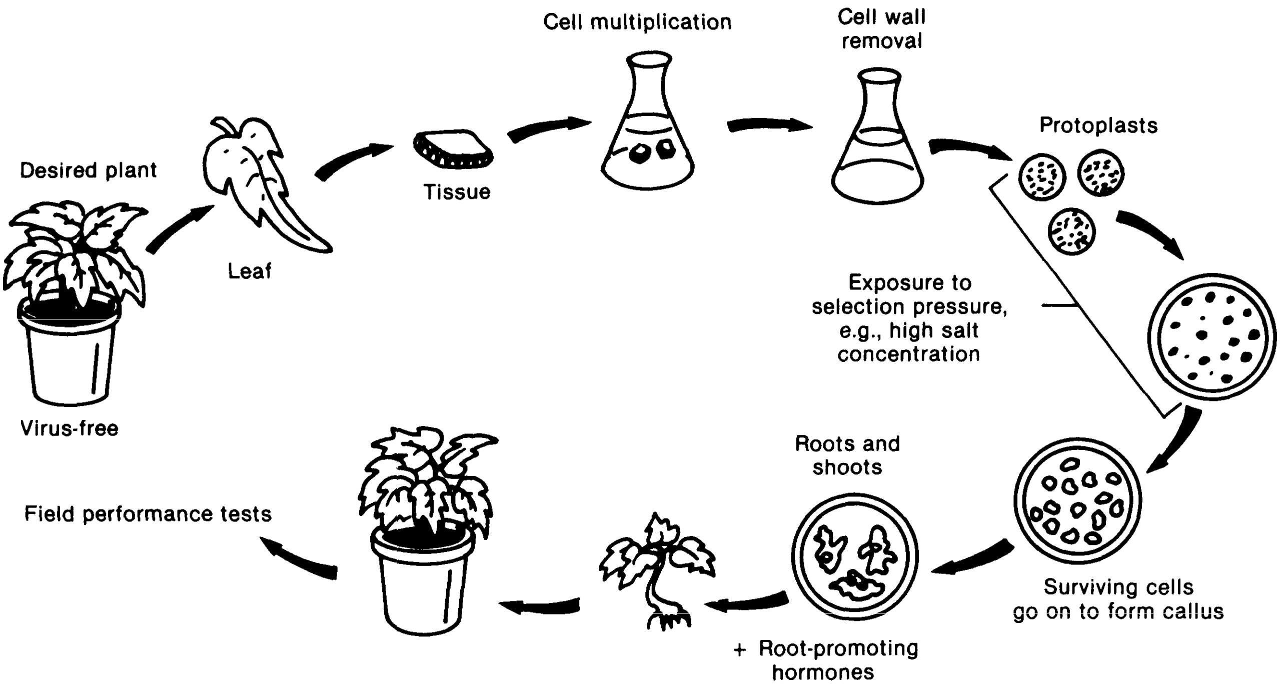
SOURCE: Office of Technology Assessment, 1988.

ment of 10 to 100 acres if individual test plants were put into the field (6).

Several species of plants can be clonally regenerated to produce genetically identical copies. The process is widely used for a range of commercial applications, including forestry and horticulture (e.g., producing strawberry, apple, plum, and peach plants). Several crop species, such as asparagus, cabbage, citrus, sunflower, carrot, alfalfa, tomatoes, and tobacco are also routinely regenerated (94). Although monocotyledonous plants, such as the cereals, have been more difficult to

Figure 10-1.—Plant Propagation: From Single Cells to Whole Plants

The process of plant regeneration from single cells in culture



The process of plant regeneration from single cells or plant tissue in culture.

SOURCE: Office of Technology Assessment, 1988.

regenerate, rapid progress is being made with these as well (1,37).

Plant regeneration is a powerful tool not only for increasing the numbers of propagated materials, but also for reducing the time required to select for genetically interesting traits. Furthermore, under certain conditions, genetic variants arise during the culturing process (somoclonal variation). Somoclonal variation can uncover new, useful variants and again reduce the time spent selecting genetically interesting traits.

Many important agricultural applications of biotechnology depend on regenerating whole plants from protoplasts. Protoplasm fusion has been applied successfully in several plants, including the potato. In this instance, cells from wild and cultivated potato plants were fused to transfer the viral resistance of the wild species. The hybrid cells were regenerated into fertile plants that expressed the desired virus-resistant characteristic (12,68). Virus-free potato cells can now be cultured in vitro, and virus-free plants regenerated; the yield of these plants has increased substantially (107). Culturing virus-free plant cells is particularly important in certain horticulturally important species, including ornamental and certain vegetable crops. As is the case with single cell or tissue regeneration, protoplasts of the monocotyledon - ous subclass of plants, such as cereals, have been much more difficult to regenerate than protoplasts of the other major plant subclass, dicotyledonous plants, such as tobacco and tomato.

Ti vectors are especially useful for genetically engineering dicotyledonous plants, such as tobacco, tomato, potato, and sunflower. For example, Ti-mediated transfer has been used to engineer virus-resistant tobacco plants (38)46) and insect-tolerant tomato plants (33) (figure IO-3). The technique is less useful for gene transfer in monocots (which include important cereal crops). Increas-

F gu e 0 2 On on Ce Bomba ded W h DNA M c op o ec es

DNA is precipitated onto the surface of 4 μm tungsten particles. A gunpowder charge in a specially designed gun detonates the firing pin that accelerates the projectiles into the onion cells. The cells remain viable if the number of particles per cell remains below 20. The DNA delivered to the cells via the particles is expressed. Three projectiles can be seen in this photograph.

SOURCE: T.M. Klein, E.D. Wolf, R. Wu, et al., "High-Velocity Microprojectiles for Delivering Nucleic Acids Into Living Cells," *Nature* 327:70-73, 1987. Reprinted by permission from *Nature*, Copyright © 1987 Macmillan Journals Ltd.

ingly, however, technical hurdles identified as barriers only a few years ago (94,101) are being cleared (1,24,43). Recent success using the ***Ti vec***tor for corn (a monocot) has been reported (43), with continued progress for monocots anticipated (108). Furthermore, direct DNA transformation apparently allows gene transfer in several cereals (monocots), including rice, wheat, and maize, with an efficiency approaching comparability to the frequency of Ti-mediated gene transfer in dicots (19).

Figure 10-3.—Genetically Engineered Insect-Tolerant Tomato Plant

Larvae were allowed to feed on a transgenic tomato plant (right) and a normal plant (left). After seven days, the plant that was genetically engineered for tolerance to **the insect is still relatively** intact, whereas the normal plant has been destroyed.

Photo credit: Monsanto Corp

New applications and new techniques, such as the "DNA plant shotgun, " (54) are continuously arising. Table 10-1 describes a few recent applications of biotechnology to plant agriculture.

Impact of Biotechniques on Agricultural Research Investment

In part, the advent of genetic engineering and related biotechniques has, itself, altered the shape and scope of U.S. agricultural research investment decisions (17)56). In particular, the emerging technologies presented fundamental challenges and opportunities for the public component of U.S. agricultural research (17). Basic science advocates charged that the USDA-led system had not been on the cutting edge of science nor had been paying enough attention to basic research (66,81), stimulating an evaluation of the system that continues today.

Some have argued that the biotechnologies have led to private sector, proprietary-dominated research efforts. Others, however, point out that increased private sector research investment resulting from the biotechnology boom has uniquely contributed to the fundamental knowledge base

Table 10-1.—Some Recent Applications of Biotechnology to Plant Agriculture

Rice: Whole rice plants can be regenerated from single-cell protoplasts; recent advances that improve the efficiency of the process are important to progress in applying genetic engineering to cereals in general (1,37).

Maize: The Ti vector was recently used to transfer the maize streak virus into corn plants, a monocotyledonous member of the grass family. The study is a landmark because the *Ti* plasmid is probably the best characterized plant vector and an efficient gene transfer mechanism, but monocots had been refractory to its use (43). Successful plant regeneration of maize protoplasts also was reported recently (80).

Rye: Using a syringe, DNA was injected into rye floral tillers. The new genetic material was introduced into the germ cells of this monocot, and some recovered seeds grew into normal plants that expressed the foreign gene. This simple strategy, which does not require plant regeneration from protoplasts, could be useful in other cereals (24).

Orange: Orange juice-sac cells have been removed from mature fruit and maintained in tissue culture. The cells produce juice chemically similar to that squeezed from tree-grown fruit. Such laboratory cultivation could advance trait selection and speed up varietal development, although laboratory produced juice is not on the immediate horizon (34).

Tomato: A gene that confers a type of insect tolerance was recently transferred via the Ti system to tomato plants. The tolerance is also expressed in progeny plants. Since over $400 million per year is spent to control this type of pest, constructing insect transgenic plants of this sort is of great interest to the agricultural community (33). See also fig. 10-3.

SOURCE: Office of Technology Assessment, 1988.

and resulted in a positive economic impact (47). And, through increasing alliances between companies and universities, industry involvement has also resulted in resources for new ideas, with potential to further enhance economic return through accelerated technology transfer (47).

Biotechnology has also stimulated greater interest in agricultural research by the nontraditional agricultural research community. Today, agricultural applications command greater interest within the general research hierarchy (23,42,89). While some believe this shift is valuable (42), others fear that research directed to address regional and local problems could suffer and that ‘(have” and “have not” institutions will result (27,52,53,58,101).

In addition to the effect of biotechnology on research investment decisions, concern has been raised about biotechnology’s influence on investment in human capital: namely, a decline in the number of full-time equivalents (FTEs) in traditional plant breeding at the expensive of increasing numbers of FTEs in molecular biology (44,58). Improvements in varieties with the new biotechniques will be hollow achievements if there is a shortage of traditional plant breeders who conduct the complementary field research that is essential to develop varieties for use by farmers. Some reports indicate a 15 to 30 percent decrease in university-based plant breeders and an increase of about one-third in molecular biologists between 1982 and 1985 (59). This trend might, in part, reflect the glamour image of plant molecular biology coupled with industrial demands for plant breeders (36).

A continuing industry demand for trained plant breeders might be an attractive argument for those making career decisions and ensure an adequate supply of plant breeders (42). However, a large majority of graduate students in the plant sciences still want to work in molecular biology, and siphoning university plant breeders to industry could leave a teaching void for those who want to learn conventional breeding (44). At present, some argue that a balance in supply seems to have been (or is being) struck (36,74). Others within industry and academia assert a lack of plant breeders exists (29,44). Regardless, evidence for both sides is largely anecdotal, and accurate accounting would be useful for forecasting and planning the direction of plant agricultural research.

The impact of the biotechnologies on the direction of agricultural research has not, however, occurred in a vacuum. Intellectual property issues and who funds projects also are important factors. For example, the concern about the exchange of plant-breeding materials just mentioned has been generated both by the research thrust using the biotechnologies and interpretation of patent law (44). The biotechniques have also contributed to an evolution in the investment emphasis (i.e., the types of projects funded) of private and public sources. The impact of these two issues, property rights and funding source, on research investment is examined in following sections.

PROPERTY RIGHTS AND PLANTS

Proprietary protection of plants precedes recombinant DNA technology by about four decades. Today, two Federal statutes specifically confer ownership rights to new plant varieties: the Plant Patent Act of 1930 (35 U.S.C. §§161-164) and the Plant Variety Protection Act of 1970 (7 U.S.C. §2321 et seq.). The ***Chakrabarty decision*** coupled with Ex ***parte Hibberd (32)*** affords plant breeders the additional option of seeking a utility patent (35 U.S.C. §101) to protect a novel variety. '

The following sections first outline the laws relevant to plant property and hybrid plants, and then analyze the effect plant protection has had on U.S. investment in agri-biotechnology. A detailed analysis of plant protection and its economic consequences will be explored in a forthcoming OTA report, New ***Developments in Biotechnology: Patenting Life.*** The issue of intellectual property as a barrier to commercializing plant products is briefly discussed later in this chapter.

Plant Patent Act of 1930 and Plant Variety Protection Act of 1970

In 1930, Congress passed the Plant Patent Act (PPA), allowing patent protection for new and distinct asexually propagated varieties other than tuber-propagated plants. PPA, administered by the U.S. Patent and Trademark Office, gives the patent holder the right to exclude others from asexually reproducing the plant or from using or selling any plants so reproduced, for a period of 17 years. At the time PPA was enacted, it was not thought possible to produce stable, uniform lines via sexual reproduction (4). These ideas were revised, however, and Congress passed the Plant Variety Protection Act (PVPA) in 1970.

PVPA provides for patent-like protection to new, distinct, uniform, and stable varieties of plants that are reproduced sexually, except fungi, bacteria, tuber-propagated plants, uncultivated plants, and first-generation hybrids. The breeder may exclude others from selling, offering for sale, reproducing (sexually or asexually), importing, or exporting the protected variety. In addition, others cannot use it to produce a hybrid or a different variety for sale. However, saving seed for crop production and for the use and reproduction of protected varieties for research is expressly permitted. The period of exclusion is 18 years for woody plants and 17 years for other varieties. PVPA is administered by the Plant Variety Protection Office, USDA.

Diamond v. Chakrabarty

In the landmark case ***Diamond v. Chakrabarty,*** the U.S. Supreme Court addressed one of the major patent law questions arising from applications of the new biotechniques—whether living, human-made micro-organisms are patentable (25). In a 5 to 4 decision, the Court made it clear that the question of whether or not an invention embraces living matter is irrelevant to the issue of patentability, as long as the invention results from human intervention. Since 1985, when the Patent Office ruled that utility patents could be granted for novel plants (32), genetically engineered plants have been granted utility patents. There are no exemptions for a plant utility patent —in contrast to PVPA, the holder of a plant utility patent can exclude others from using the patented variety to develop new varieties.

Impact of Intellectual Property on Agricultural Research Investment

Intellectual property and plant protection have influenced and continue to influence the direc-

[1]Trade secrets are also an important form of plant protection. In particular, the hybrid seed industry (such as corn) makes extensive use of trade secrets (36). Hybrid seeds have "internal genetic protection, " making them more amenable to the trade secret approach (27). Inbred parental lines (trade secrets themselves) are cross-bred to produce high-yielding hybrid seed (also trade secrets) with 'hybrid vigor." But, unlike seed for nonhybrid crops, seed from a harvest using hybrid seed cannot be saved and used for additional high-yield planting cycles. Since hybrid vigor from subsequent progeny declines, the producer must return to the source for new seed to maintain the highest yields. Thus, the genetics of hybrid seed *de facto* force the producer back to the supplier, and the hybrid seed industry has preferred trade secret plant protection, rather than seeking monetary return through the certificate or patent process (each with disclosure requirements) (26). Academic researchers probably view trade secrets less favorably, since they hinder publication efforts (94).

tion of U.S. plant agricultural research investment. Since the enactment of PVPA and the ***Chakrabarty*** decision, private sector interest has blossomed (101). Funding to initially capitalize dedicated biotechnology companies (DBCs) was based, in some measure, on the expectation that legal means existed to protect discoveries resulting from the investment. In particular, some view the option of applying for plant utility patents (afforded by ***Chakrabarty*** and Hibberd) as sparking progress and increasing dollar flow in the industry by providing both the scope of protection needed to encourage new research investment and the rapid dissemination of information describing the new technology resulting from the research (109).

In contrast with the ***Chakrabarty*** decision, the role of PVPA in directly stimulating private investment is less clear (18). Some argue that the rate of private research investment in plant breeding following passage of PVPA equals that during the preceding decade (55), However, others dispute the notion that private investment has not risen since passage of PVPA in 1970 (61)63). The perception, however, that PVPA would increase the profitability of seed companies galvanized far--reaching acquisition and merger activity involving many American and international companies (18,55). These corporate entities were then poised to take advantage as events in the biotechnology revolution unfolded.

Plant protection is not only important to commercial parties, but to public sector institutions as well. Until 1980, only about 4 percent of some 30,000 government-owned patents were licensed (73). Furthermore, the government policy of granting nonexclusive licenses discouraged investment, since a company lacking an exclusive license was reluctant to pay the cost of developing a product and building a production facility. Potentially valuable research thus remained unexploited. Congressional concern about this innovation lag prompted passage in 1980 of the Patent and Trademark Amendment Act (public Law 96-517), with amendments in 1984 (Public Law 98-620) to encourage cooperative relationships between universities and industry, with the goal of putting government-sponsored inventions in the marketplace. Burgeoning university-industry relationships have been attributed, in part, to patent policy (101).

On one hand, intellectual property rights stimulated and are critical to maintaining investment—public and private–in plant biotechnology research. Innovation must be protected and rewarded to realize a continuing flow of dollars to agri-biotechnology R&D (30,109). On the other hand, many individuals are concerned that increased patent activity is having serious and adverse consequences resulting in the "privatization" of agriculture (17,26)56). Greater awareness of potential profits to be accrued from patenting genes and products has led to a rush to register under the existing patent laws (30). Moreover, patenting in biotechnology is increasingly viewed as a defensive mechanism (42) to protect future investment and projects, rather than a means that expects immediate return.

To many in both the public and corporate sectors, increased patent activity is tying up, or has the potential to tie up, germplasm (28,30,44). Some argue that a noticeable slowing in the free exchange of germplasm that existed prior to patenting has occurred (28,44). In effect, they argue that the biological domain was once public domain, but has shifted to a private property right (27). Others argue that utility patents do not stifle free exchange (109). Rather than patents ***per se,*** recognition that germplasm is commercially valuable could be resulting in closer attention being given to free transfer (75). In any case, advances in both plant breeding and plant biotechnology require free-moving, international exchange of germplasm.

AGRICULTURAL BIOTECHNOLOGY RESEARCH FUNDING

The U.S. agricultural research enterprise is a system. Lodged partly in the private sector and partly in the public sector, it is comprised of a broad variety of institutions funding both traditional and biotechnological research in agriculture. In response to scientific, legal, economic, and political pressures, the system evolves, seeking to balance the diverse requirements and interests of each stakeholder. At issue is how research will be prioritized, what lines of research should be pursued, and what research roles are appropriate for the respective public and private sectors. This section examines who invests in plant biotechnological research in the United States and to what extent the funding source (e.g., Federal Government, public institutions, private corporation) influences the direction of agricultural research. (For a detailed accounting of biotechnology funding, see chs. 3,4, and 5, and for agricultural funding in general [681.)

Public Investment

U.S. public investment in agricultural research involves two principal partners: the Federal Government and the States. Within the Federal sector, USDA funds the majority of plant research. In addition to the USDA, other Federal agencies, including the National Science Foundation (NSF), National Institutes of Health (NIH), Department of Energy (DOE), Agency for International Development, Department of Defense, and National Aeronautics and Space Administration, support basic science research on or applicable to plant biotechnology. NSF in particular, funds many basic research initiatives and training programs in the plant sciences. In the more recent past, NH-I and DOE played critical roles funding basic plant researchers at non-land-grant institutions.

Funding for all agricultural research by the public sector is estimated at approximately $2.0 billion–$1.9 billion combined Federal and State support of the traditional USDA system and $100 million through grants from other agencies (68). Not all of this research, however, involves plants or biotechnology. The following sections describe plant research initiatives within the public sector and, where available, plant biotechnology applications. Targeted investment in education and training is also presented.

U.S. Department of Agriculture

A long tradition and a complex institutional funding structure characterize agricultural research investment by USDA. Most federally sponsored research in plant biology is conducted at land-grant institutions, which are part of a tripartite USDA complex that includes 72 land-grant institutions, 146 State agricultural experiment stations, and thousands of extension agents (one in virtually every county in the United States).

Determining the precise amount of USDA funding in plant biotechnology is problematic. Funding amounts for plant science or biotechnology projects are generally distinguished, but not both as a unit. Nevertheless, it appears that the majority of research funding obligated by USDA involves plant applications (103,105, 106).

USDA allocates research funds through the Agricultural Research Service (ARS) for intramural research, the Cooperative State Research Service (CSRS), and the Office of Grants and Program Systems for competitive grants funding. ARS sponsors in-house research allocated among 140 intramural research facilities located nationwide. CSRS distributes funds based on a formula incorporating each State's farm and rural population. CSRS-sponsored research is carried out largely at State agricultural experiment stations and colleges of veterinary medicine that are part of land-grant universities. CSRS funding includes a State-matching formula. Competitive grant funding by USDA was established nearly a century after initiation of the land-grant complex, and expenditures are not limited to land-grant institutions.

Within ARS, approximately 38 percent of research dollars (fiscal year 1986 appropriation of approximately $185 million) are specifically designated for plant science (106). The Competitive Research Grants Program of CSRS does break out plant biotechnology. Plant applications were 58 percent of funds for competitive grants awarded; biotechnology applications 45 percent; and plant biotechnology applications 28.5 percent (total budget $40.1 million) (105). Table IO-2 describes some of the kinds of projects funded by the CSRS competitive grants program.

In education and training, land-grant universities also support 80 percent of the Nation's plant biology faculty and graduate students (68). USDA funds 200 to 300 graduate students at both land-grant and non-land-grant institutions through training grants in four targeted areas, one of which is biotechnology (68). USDA also has a modest com-

Table 10-2.—Examples of USDA Competitive Grants Awarded for Plant Biotechnology

- Molecular Cloning of a Rubber Gene From Guayule
- Cloning of Maize Regulatory Genes
- Molecular Biology of Rice Genes
- Regulation of Soybean Seed Protein Gene Expression
- Organization and Manipulation of Wheat Storage Protein Genes
- Delivery of DNA Into Cells of Onion and Tobacco Using High Velocity Microprojectiles
- In Vitro Culture of Cool Season Forage Grasses
- Molecular and Genetic Studies in Barley
- Identification of DNA Markers for Disease and Pest Resistance in Potato
- Molecular Biochemistry of Herbicide Resistance
- Regulation of Cytochrome Synthesis in Photosynthesis
- Directed Mutation Studies of the Photosynthetic Cytochrome b6
- Regulation of Corn Nitrate Reductase: Application of Monoclinal Antibodies
- Regulation of Nitrite Reductase

SOURCE: U.S. Department of Agriculture, Office of Grants end Program Systems, Cooperative State Research Service, *Food and Agriculture Competitively Awarded Research and Education Grants, Fiscal Year 1986,* Washington, DC, 1987.

petitive postdoctoral fellowship program through ARS. Of the approximately 100 fellowships awarded in fiscal year 1986, about one-half were in biotechnology (68). CSRS funds Food and Agriculture Sciences National Needs Graduate Fellowship grants that supported 87 doctoral degree candidates (many in plant fields) in fiscal year 1986 (105).

National Science Foundation

NSF plays a pivotal role in funding basic plant biological research, training, and education. In fiscal year 1985, NSF awarded 50 percent of competitive Federal funding for plant research (71). In addition to research investment, agency expenditures are also devoted to developing the plant sciences human resource base. For example, NSF conducts a peer-reviewed, competitive postdoctoral plant biology fellowship program that emphasizes an interdisciplinary approach to expand an individual's training into plant biology -e.g., bacterial molecular biology to plant molecular biology. The program provides funds for approximately 20 fellows per year. NSF also sponsors a summer course in plant molecular biology for 16 scientists each year (68).

Science and Technology Centers for Plant Science

Plant biotechnology is one of several relevant research areas that could be covered at proposed multidisciplinary plant science research centers to be funded jointly by USDA, NSF, and the Department of Energy. The proposal initially will involve $10 million per year and use a competitive grant/peer review process to establish several centers with average annual funding of $1 to $2 million per center for 5 years. The Administration's Working Group on Plant Science believes that $250 million during the first five years of the program represents a realistic recognition that the scant amount of competitive funding for plant sciences needs to be increased or the search to elucidate many fundamental principles of plants will continue to lag (79). Collaborative arrangements (including funds, equipment, or people) between State and local governments, private foundations, and industries would be encouraged, although the grantee must be a doctorate granting institution with graduate programs related to plant sciences. Proposed centers are encouraged to form, wherever possible, research and training relationships with existing facilities, such as those of the Agricultural Research Service and National Laboratories (72).

States

States play a significant role in funding agricultural research, plant biotechnology included. One analysis reports that in 1985, the ratio of State to Federal appropriations through CSRS at State agricultural experiment stations was 3.5 to 1 (68); another estimates that the ratio is much less, approximately 2 to 1 (62). Total expenditures by State legislatures for State agricultural experiment stations approach $700 million annually (68). In addition to State contributions through CSRS, some States, such as Iowa, have targeted agri-biotechnology as a strategic industry for State investment (see box 10-B).

In addition to research and facilities funding, States have also recognized the importance of investing in human capital. For example, Iowa and North Carolina have special graduate and postgraduate fellowships in plant molecular biology.

Box 10-B.-Biotechnology in Iowa

"All encompassing" probably best characterizes the biotechnology effort underway in Iowa. Involving the State's executive and legislative branches, industries, and colleges and universities, the necessary components of a multi-faceted approach for success are each seemingly covered. These include:

- 2-year laboratory technician training,
- undergraduate biotechnology training,
- graduate biotechnology training,
- faculty development and recruitment,
- equipment acquisition,
- facilities improvement and new construction,
- tax incentives for industry R&D, and
- programs for employee training.

These efforts are targeted primarily toward agriculture, the State's principal industry.

Several State initiatives help ensure the availability of adequate personnel. In response to the needs of companies, a 2-year laboratory technician training program has been designed at Iowa Valley Community College. The program focuses on developing human capital skilled in recombinant DNA and monoclonal antibody technologies (39). The corporate-sponsored Undergraduate Agricultural Biotechnology Scholarship Program at Iowa State University (ISU) provides up to full-tuition scholarships for students. In 1984, the University of Iowa (UI) established the Iowa Biotechnology Training Program, funded by a competitive grant from the USDA (39). The program leads to a Ph.D. in microbiology or immunology (16). UI is also home to the Biocatalysis Research Group, an endowed graduate program (M.S., Ph.D.) that focuses on biocatalysis and bioprocessing (39,82). Finally, UI also awards degrees in chemical and materials engineering with an emphasis in biochemical engineering and biotechnology (110). The program provides coursework and research opportunities at the B.S., M.S., and Ph.D. levels (110).

In addition to student initiatives, faculty support has been enhanced. For example, at ISU a $1 million Pioneer Hi-Bred International Endowed Chair in Molecular Biology of Maize was established. A $400,000 grant awarded to ISU by the Northwest Area Foundation in 1984 allowed the creation of two new faculty positions in the genetics department (51).

Support for biotechnology extends beyond the universities to the State's government officials. The Iowa legislature has committed $18 million to Iowa State University for agricultural biotechnology research over the next 4 years (39). A half million dollars from State lottery funds were earmarked in fiscal year 1986 for biotechnology training, and $3.75 million in fiscal year 1987 for research funding (39). The legislature and governor have also supported building and equipment funding for ISU and UI (9,40,41,85,86).

Local and international businesses, such as Darst/Imperial Chemical Industries and Pioneer Hi-Bred International, play central roles in Iowa's biotechnology push—funding projects at the universities and interacting with government to optimize the State's biotechnology climate. Iowa offers a property tax abatement for businesses that expand their research activities, and the Iowa Jobs Training Program, developed in 1983, pays up to 50 percent of employees' salaries and as much as 100 percent of instructors' salaries for up to a year. Funds can also be used for specialized employee training worldwide. Companies that expand their work force by at least 10 percent, or those starting a new enterprise using the state training program, are eligible for a State income tax credit of more than $700 for each new employee (39).

The State's efforts to highlight its biotechnology industry are innovative and global. In Fall 1987, the State's Department of Economic Development, UI, and ISU sponsored a "Biotech Express Dinner Train" from Ames to Iowa City. Designed to highlight Iowa's biotechnology industry, State officials invited 300 American and 300 Japanese business executives for the 3-day affair (9).

It is too early to evaluate the overall success of Iowa's efforts. It is clear, however, that the concerted and intensive biotechnology initiatives underway are impressive, but no more so than the high-yield expectations. In his 1987 "State of the State" speech, Governor Terry Branstad stated, "Biotechnology will change the world, giving us new tools in crop and livestock production and processing. For a $35 million investment, Iowa State University officials are confident we will attract over $120 million in research to Iowa over the next decade . . . . They [the State's universities] are poised to help Iowa lead the nation in moving . . . to the age of . . . biotechnology" (11).

SOURCE: Office of Technology Assessment, 1988.

State universities outside the land-grant complex also are pivotal to research and training in plant biotechnology.

Combining matching funds and novel initiatives, the bulk of State investment in biotechnology is probably related to plant agricultural applications—at least 33 States have biotechnology initiatives (ch. 4), many with plant agriculture components (table 10-3).

Private Investment

Private funding for agricultural research derives primarily from industry, although private foundations, trade associations, and commodity organizations also channel money into the system. Companies also provide money to universities for doctoral and postdoctoral education and training,

Dollar expenditures for agricultural research by the private sector are difficult to determine, One recent survey places industry funding at approximately $2.1 billion (2), and it may approach $3 billion (101). Again, not all of this research involves plants or biotechnology, but, in the past few years, investment in plant research using genetic technologies has accelerated in both the private and public sectors (7). The following sections describe plant research and education investment by private sector interests, with particular focus, where available, on plant biotechnology.

Industry

Commercial funding of plant biotechnology research derives from two sources: large (often multinational) corporations and dedicated biotechnology companies (DBCs) (ch. 5). In a 1987 OTA survey of nearly 300 DBCs, 12.5 percent indicated plant agriculture as a primary or secondary focus. Corporate biotechnology companies (CBCs) involved in applications of biotechniques to plants are largely fully integrated seed companies. Research investment includes both intra- and extramural funding.

Table 10.3.–State-University Research Center Initiatives in Plant Biotechnology

State	Description
Georgia	State Legislature appropriated $7.5 million for the construction of a $32 million Center for Biotechnology at the University of Georgia. Research emphasis will focus on cattle, hogs, and peaches.
Indiana	Indiana Corporation for Science and Technology specifically targets biotechnology and agricultural genetics as 2 of 13 strategic areas. The Corporation has granted over $2.5 million for biotechnology projects at the Agrigenetics Center at Purdue University or the Molecular and Cellular Biology Center at Indiana University.
Iowa	State Legislature appropriated $18 million over four years to Iowa State University for agri-biotechnology research. See also box 10-B.
Maryland	Center for Advanced Research in Biotechnology established at the University of Maryland with agriculture as one of five research areas.
Michigan	Michigan Biotechnology Institute established at Michigan State University includes focus on plant genetic engineering and tissue culture projects related to forestry and new uses of agricultural surpluses.
Missouri	Food for the 21st Century Center established at the University of Missouri, Columbia.
New Jersey	Center for Advanced Food Technology established at Cook College, and the Center for Agricultural Molecular Biology established at Rutgers University.
New York	Biotechnology Institute created at Cornell University. New York State Science & Technology Foundation also has designated Cornell University a “Center for Advanced Technology.” The agriculture and food industries are target areas of both programs.
North Carolina	North Carolina Biotechnology Center established, targeting agriculture and forestry as part of its R&D program. Center also offers graduate and post-graduate fellowships in plant molecular biology.
Ohio	Edison Animal Biotechnology Center established at Ohio University and the Biotechnology Institute at Ohio State University.
Oklahoma	21st Century Center under construction ($30 million) at Oklahoma State University, Stillwater. Focus of center will be agricultural biotechnology, water resources, and renewable energy.
Pennsylvania	Cooperative Program in Recombinant DNA Technology established at Pennsylvania State University. Penn State Biotechnology Institute established with agricultural biotechnology one targeted research area.
Washington	Washington Technology Center established. Projects funded include livestock, crop, and forestry applications of biotechnology.
Wisconsin	Biotechnology Center established at the University of Wisconsin, Madison includes a Plant Cell and Tissue Culture Service Facility. A high containment growth chamber for recombinant plants also is being developed.

SOURCE: Office of Technology Assessment, 1988.

Industry also recognizes the importance of supporting the manpower base for the plant sciences. For example, several companies, such as Ciba-Geigy, have established in-house postdoctoral training programs, Graduate and postgraduate students have benefited from Agrigenetics' investment at several university laboratories.

Philanthropic

Noncorporate private sources, including foundations, trade associations, and commodity organizations, invest in some agri-biotechnology research. The nature of the funded projects varies with the interest and purpose of the organization. Although the money usually supports research, funds are sometimes earmarked for training and education. For example, in 1982, the McKnight Foundation of Minneapolis announced plans to spend $2 million a year for the next 10 years on basic research and graduate education in plant biology. Most of that money is targeted for about a half dozen universities, with interdisciplinary research teams focusing on plant genetics. Grants will consist of up to $300,000 a year for the support of doctoral and postdoctoral research. An additional ten grants of $35,000 per year for 3-year periods will be awarded to university scientists conducting basic research in plant biology related to agriculture. Despite such efforts, philanthropic investment is modest compared to the funds available from public sources.

Collaborative Arrangements

The typology and purposes of collaborative arrangements (see ch. 7) in plant agricultural biotechnology apparently do not differ from other sectors. Industry interaction with land-grant institutions has a long tradition within the agricultural sector (23,78), although the number of formal collaborations between agricultural biotechnology companies averages one to two per company in contrast to seven or more for the human therapeutics sector (8).

Today, collaborative arrangements in plant agricultural biotechnology include university-government, university-industry, and university-industry-government associations. For example, State-university cooperation in agri-biotechnology has been manifest in the establishment of several research centers with plant biotechnology components (table 10-3). In addition to government-university interactions, several dedicated and corporate agri-biotechnology companies make grants or other arrangements with university researchers or research groups, Table 10-4 lists some types of projects that companies have funded, or presently fund, at universities. An ambitious consortium involving collaboration between universities, industry, and Federal and State Governments recently has been inaugurated (see box 10 C). Finally, a cooperative project, the Biotechnology Research and Development Corp., involving the USDA, several companies, the State of Illinois, and the Peoria Economic Development Council was recently formed (10).

Impact of Funding Source on Agricultural Research Investment

Historically, public investment in agricultural research has been through the land-grant system. Land-grant institutions were established on a public service basis different from that of other universities, with a tradition of an implied social contract to make its discoveries freely available to the public (101), Since 1965, however, federally funded agricultural research through formula funds and USDA has remained stagnant or declined (in constant dollars), while State and private sector support for agricultural research has increased significantly in real terms. Private sector investment now exceeds public funding. And, within the public sector, the funding structure is evolving. Has the changing funding mix influenced agricultural research investment?

Formula-based Funding v. Competitive Grant Funding

As mentioned earlier, charges have been leveled that the USDA research enterprise has not been at the cutting edge of science. Such criticism often focuses on the tradition of formula funding. In response, a competitive grants program has been established by USDA (93). The peer-reviewed, competitive grants program allows non-land-grant universities to participate in research thrusts funded by USDA. Peer review at ARS was recently

Table 10-4.—Types of Private Plant Agriculture Grants to Universities

Funding Source	University	Project Description
Agrigenetics Corp.	Cornell	Tomato hybridization through cell culture
Asgrow Seed Co. (Upjohn)	Purdue	Soybean research
Busch Agricultural Resources, Inc.	U. Arkansas	Rice breeding, genetics, and evaluation
Chocolate Manufacturers Assn.	Purdue	In vitro production of cocoa
Cotton, Inc.	U. Arkansas	Development of types of early maturing cotton for Eastern Arkansas
Crow's Hybrid Corn Co.	Cornell	Tissue culture regeneration
Dow Chemical	Purdue	Soybean plant regulation
Eli Lilly & Co.	Purdue	Wheat genetics research
Hershey Foods	Penn. State	Molecular biology of the cocoa plant
Monsanto	Rockefeller U.	Regulation of plant genes involved in photosynthesis
Nestle	Cornell	Bitterness in squash
North American Plant Breeders	Purdue	Evaluation of alfalfa and red clover varieties
Northrup King (Sandoz)	Cornell	Tissue culture regeneration
Pioneer Hi-Bred	Penn. State	Regulation of grain yield in maize
Popcorn Institute	Purdue	Improvement of popcorn hybrids
Quaker Oats	Purdue	Improvement of competitive ability of oats in Indiana and other Midwestern States
Rohm & Haas	U. Penn.	Support for Plant Science Institute
Showalter Trust	Purdue	Development of tissue culture systems to produce plant secondary products
Standard Oil	U. Illinois	Long-range improvement of food production, primarily in corn and soybeans
Upjohn	Purdue	Muskmelon breeding program

SOURCE: Office of Technology Assessment, 1988.

reviewed, and recommendations were made to strengthen the process in several ways (69).

The move to a competitive agricultural research program has led to concern that elite, well-staffed institutions will be favored. Critics charge that the peer review system that is generally used has resulted in the top 20 research universities receiving the bulk of Federal research dollars year after year (92). Under the grant process at the National Institutes of Health, critics point out 1 to 2 percent of institutions receive as much as 20 percent of the funding. With geographical considerations such an important part of the agricultural research sector, concern has been and continues to be expressed that the valuable research functions performed by the smaller land-grant institutions would increasingly receive less attention.

While sensitive to such concerns, others maintain that allocation of new and even redirected resources from USDA should be based primarily on competitive peer and merit review. They argue that such a system ensures that public dollars are invested most wisely and efficiently without limiting the character and diversity of U.S. agricultural research (68)93). These individuals contend that while there appears to be a threat to the system, the long-term impact will be beneficial, leading to a more competitive science and a more competitive industry (74).

Because competitive grants represent, at present, less than 5 percent of the USDA agricultural research budget, it is difficult to assess their impact, both on concerns raised and expectations held.

Box 10-C.--The Midwest Plant Biotechnology Consortium

The Midwest Plant Biotechnology Consortium (MPBC) is the first, and operationally most advanced, university-government-industry consortium to focus on agricultural applications of biotechnology. MPBC represents 15 midwestern universities, three Federal laboratories, 37 agribusiness corporations headquartered in the Midwest, and research institutes from eight States: Illinois, Indiana, Iowa, Michigan, Minnesota, Missouri, Ohio, and Wisconsin (29). While formally not participants in the MPBC, the Department of Energy, USDA, National Science Foundation, and National Institutes of Health have expressed interest in the technical, organizational, and economic purposes of the consortium (29).

The purposes of the MPBC are two-fold: to carry out basic research in plant biotechnology and to promote the transfer of that technology to foster economic competitiveness of U.S. agriculture and agribusiness. The issues and needs addressed by the MPBC encompass midwestern crops and cropping practices, particularly in the areas of plant growth, plant storage, pesticides and herbicides, processing, and seeds. Much of the basic research, however, on plants like corn and soybeans is relevant to other species (29).

Operating on the premise that a planned, coordinated basic research program on the biochemistry, physiology, molecular biology, and biophysics of plants—fields of interest to area universities and Federal facilities—can make major contributions to commercial biotechnology, the participating nonindustry members collaborated to prepare research preproposals in response to identified needs. The industrial participants of the MPBC then reviewed the preproposals and selected those with highest industrial relevance. The preproposals have been developed into full proposals, and are undergoing scientific peer review by individuals outside the Midwest and the MPBC (29). After completion of the review process, those with greatest technical merit will be submitted as the MPBC proposal to the USDA competitive grant process for Federal start-up funding (29).

The industry members of the MPBC have provided the initial cash for the consortium's policy and operating secretariat. Federal and State matching dollars are expected to fund the MPBC, with State funding used only for institutions within the State. Funds would be used primarily for training and support of students, fellows, and technical staff, not facilities or capital equipment. After five operating years, the entire project will be reviewed and continued only if its purpose of providing a fundamental research base to facilitate technology transfer is being met (29).

An important aspect of the MPBC is recognition that the basic knowledge foundation of plant biology necessary for commercial breakthroughs to new biotechnological products is lacking, and that this type of research funding is most appropriately provided by the Federal Government (29). Any intellectual property rights resulting from such research will reside with the research participants, as governed by the individual's institutional practices. Industrial members of the MPBC, however, would have access to the first disclosure of information, with further development pursued between the interested parties (29).

The MPBC is a rather unique collaborative effort in biotechnology, and certainly *in plant* biotechnology. Although the MPBC is organizationally one of the more advanced consortium endeavors, it is still embryonic. And while participants are optimistic about a prosperous future, antitrust obstacles must still be overcome (29). Nevertheless, the concept of enhancing U.S. competitiveness in agriculture, agribusiness, and biotechnology through a university-government-industry collaborative arrangement shows promise.

SOURCE: Office of Technology Assessment, 1988.

Increased Commercial Involvement

Agribusiness in the United States today is changing—becoming bigger, and also more horizontally and vertically integrated (101). Historically, corporate research programs are driven by the economic incentive to produce a profit-yielding product. In the case of plant biotechnology, however, private investment in basic research was necessary to enhance the paucity of knowledge available about plant systems. This increased spending by the commercial sector was coupled with real dollar declines in Federal support (28).

Some believe that an overall weakening of the public sector role in agricultural research, especially within the land-grant complex, and a corollary strengthening of the position and interests of the private sector is occurring, and that this could portend problems. For example, strengthening support by the private sector could present problems in intellectual property or developing technology of real benefit for farmers (62). Arguments also have been raised that an erosion of the public interest in agricultural research might not be in the best interests of the Nation if high-cost/high-yield projects are pursued, rather than low-input/low-cost options (28).

In addition to the increased money being spent by industry, a recent flurry of merger activity involving agribusiness has also raised questions about the direction of agricultural research investment. Since the late 1960s, seed companies increasingly have become subsidiaries of larger corporations, especially chemical firms. Some express concern that consolidation of seed and agrichemical companies will make projects such as herbicide-resistant plants attractive, and that such applications will lead to increased dependence on chemicals also produced by the same firm.

Others point out that private investment in agri-biotechnology is vital to the country's economic well-being and will enhance the global position of American agriculture in the world marketplace through low-input options. It is also argued that the opportunities afforded by private involvement in agri-biotechnology could produce health and environmental benefits through industrial efforts to develop products that decrease the present dependence on chemical pesticides and herbicides and lead to more efficient nonchemical control methods.

Private spending on agri-biotechnology cannot, however, replace public involvement. Private support for basic research, intramural and extramural, is expected to decline (95) as companies increasingly identify potential products and shift funding toward applied R&D. Industry can, however, act as an advocate for public funding of agri-biotechnology research (68) as it looks to public investment for advances in fundamental research. Because universities are well-springs of innovation, commercial agriculture will benefit from collaborative arrangements that support basic research. (Questions surrounding such collaborative arrangements are discussed in ch. 7.)

Resource Allocation Within USDA

Public investment in agricultural research is necessary because incentives for private research are often inadequate. The social return could be considerable, but private profit is meager, with gains captured by other firms, by producers, and by consumers (84).

Implied in public funding of agricultural research is responsibility to the public, which is entitled to broad benefits. For example, historically Black colleges of agriculture in the land-grant system have important programs targeted to smaller farms. Yet today, the USDA-led enterprise is increasingly challenged by consumers, environmentalists, farmworkers, and rural development advocates who have a range of concerns and research priorities. Concern about land-grant accountability led to a lawsuit in California examining the role and impact of federally funded research. In November 1987, a verdict, which is being appealed, was issued ordering the University of California to develop a process to ensure that Federal Hatch Act appropriations are used to enhance rural life and promote small family farms (13).

Over its long history, public research has demonstrated that it contributes to the maintenance or enhancement of a competitive structure in the agricultural production, farm supply, and marketing sectors (84). Concerns recently have been raised, however, that the U.S. public agricultural research system lacks focus toward equity for farmers and consumers, and that an examination of priorities could be necessary (26).

USDA's Users Advisory Board has recommended that public sector research should encourage strategies that increase profitability, reduce the need for subsidies, protect the environment, and enhance rural development and world competitiveness (106). With or without biotechnology, public sector agricultural research institutions could emphasize biological processes and cultural management in the field, new crop diversification, and host-based disease and insect resistance for crops, Most agree—in both the commercial and public interest sectors—that U.S. agricultural research programs need to be revitalized and recredited in the public's mind. This issue is paramount if the USDA system is to reap maximum benefit.

COMMERCIALIZATION OF AGRICULTURAL RESEARCH

The United States' ability to transfer technology-including agricultural technology-from laboratory to marketplace is under increasing scrutiny. Generic issues described earlier also apply to commercialization of plant agricultural biotechnology as well (see chs. 5 and 6). For example, collaborative arrangements have been designed to enhance commercialization of plant biotechnology research. What is the general profile of commercial plant agricultural biotechnology, and what issues are important to product development in this sector?

As mentioned earlier, about one-eighth of DBCs (37 companies) surveyed by OTA in 1987 are involved in R&D of plant agricultural applications. The OTA survey also found that the profile of patent activity for these companies was similar to that for DBCs in general (see chs. 5 and 6). Including corporate participants, the commercial sector for plant agricultural biotechnology does not appear to have changed appreciably since a 1984 OTA report of industry activity (94).

Nevertheless, expectations for profitable returns on investment in agri-biotechnology are high. Estimated revenues from world seed sales range from $30 to $60 billion (6,7), with the U.S. share representing approximately one-fourth the world market (7). Some analysts predict that, with genetically modified seeds, the world market could reach $150 to $180 billion by 1990 (6), and that disease-, pesticide-, and herbicide-resistant plants could constitute a sizable portion of the $10 billion agricultural chemical market (6). Others are less optimistic, but still see real growth, anticipating a slow to moderate growth rate (5 percent annually) over the next decade (7). This represents a doubling between 1982 and 1995 (7). Yet, compared to human therapeutics, raising adequate capital for research has been relatively difficult for most agricultural biotechnology companies, including plant biotechnology firms (76). However, the world-wide nature of agriculture could result in biotechnological agriculture processes and products, both plant and animal, becoming the largest sector in the industry (64,65). Table 10-5 lists one analysis of probable years of commercialization for several genetically manipulated crop plants.

To achieve success under either growth pattern, widespread commercialization of plant biotechnology will require breakthroughs in several technical areas. It will also depend on other factors, including environmental regulation, university-industry relations, economic incentives, and consumer acceptance. A comprehensive analysis of the commercial plant biotechnology sector is beyond the scope of this chapter. As a case study, however, two issues specific to commercialization in the plant biotechnology sector merit discussion: institutional barriers to development and personnel needs.

Table 10.5.—Probable Year of Commercialization for Some Genetically Manipulated Crop Plants

Tomatoes	**1988**
Other vegetables	1989
Potatoes	1989
Sugar cane	1989
Fruit	1990
Rapeseed	1991
Rice	1991
Sunflower	1991
Alfalfa	1992
Barley	1992
Corn	1992
Sorghum	1992
Soybeans	1992
Wheat	1992

SOURCE: M. Ratafia and T. Purinton, "World Agricultural Markets," *Bio/Technology* 6:280-281, 1988.

Institutional Barriers to Development

Practical use (through public or commercial availability) of plant agricultural research is ingrained in the fabric of the U.S. system. Although this chapter focuses primarily on aspects that affect investment in U.S. agri-biotechnology research, it is also important to delineate parameters that influence the flow of plant biotechnology products to the open market. The following three sections analyze three parameters identified and examined at a 1987 OTA workshop (95), that are impeding or could impede rapid plant biotechnology development: the existing knowledge base, regulation, and property rights.

Knowledge Base

While an enormous information base has provided a substructure for sweeping advances in biomedical science (68), similar basic knowledge about plants and plant systems is in short supply. Experts from academia and industry nearly all agree that the sparse fundamental knowledge base underlying plant agricultural biotechnology, especially in crop species, is the rate-limiting barrier to commercial development, and that developing the base is critical to future U.S. efforts (95).

The level of basic scientific knowledge about plants is rudimentary and limited to certain species (89). Basic biochemistry of plants and plant systems is poorly understood. For example, the metabolic basis of drought resistance is not understood, let alone the genetics of this trait. The same holds true for many plant traits. Knowledge about gene expression and developmental regulation of plants is not well defined, and while plants are a major source of pharmaceuticals and other specialty chemicals (45,94,99), biotechnological applications are poorly exploited; only one product is currently under production (45)87). At the plant molecular level, only a few important plant genes have been cloned and sequenced (67), and complete molecular maps to correspond to genetic maps are available for only two or three species (36,42).

A comprehensive treatise on the knowledge gaps in plant sciences is beyond the scope of this chapter, however, table 10-6 lists some basic research needs in plant biotechnology. A following section analyzes the division of labor between the public and private research sectors to meet these needs.

Table 10-6.-Some Knowledge Gaps in Plant Agriculture Needing Basic Research

- Gene, seed, embryo libraries and banks
- Model systems to correlate with important crop species
- Metabolic regulation and expression of polygenic traits
- Germination: storage, differentiation, and properties of embryonic tissue
- Plant differentiation: morphology and physiology for all stages
- Gene structure and function
- Biochemistry and mechanisms of plant regulators and hormones

SOURCE: Office of Technology Assessment, 1988.

Regulatory Uncertainty

Government regulates commerce for a wide range of reasons, including protection of human health and the environment. State initiatives and the Federal regulatory structure for biotechnological products were analyzed in a previous OTA report (96). Does the present regulatory environment act as an institutional barrier to commercial development of plant biotechnology?

Regulatory uncertainty stands as the second major barrier to commercialization of agricultural research (95), and could become the most serious (28,36)42,47,78), For the agricultural sector of the biotechnology industries in particular, regulatory delays have hampered the movement of products from laboratories and greenhouses, to small-scale, experimental field tests (20). While the furor appears greater when the application involves micro-organisms, genetically engineered plants with bacterial or fungal genes also have been tied up in the regulatory system (20,96).

Routine progress toward field and environmental testing of genetically engineered organisms has been slow, with controversy and confusion among Federal regulatory agencies leading to uncertainty within the biotechnology research community and industry (68). This uncertainty has resulted in significant delays in field research on potential agricultural biotechnology products (68). Dissatisfaction with Federal regulation of biotechnology (both too much and too little) has focused on the two agencies that regulate agricultural products: USDA and EPA (20).

From a commercial standpoint, Federal regulation needs to be affordable and should support, not stifle, technology development (36). Unanticipated regulatory delay can dramatically affect the profitability of products and the commercial agricultural biotechnology research agenda (47). Regulatory uncertainty, for example, affects decisions by companies on whether to spend $1 to $2 million on greenhouses only because of concern over future field tests v. greenhouse work, instead of investing the money in research (42).

In contrast to regulatory delay for pharmaceutical biotechnology, crop agriculture is particularly sensitive to a time lapse. A one-month delay at a critical time can result in a lost year of development. A one-year delay can reduce profit by 50 percent during the product lifetime and stem cash flow (47). Missing a seasonal planting window for an experimental field trial of a plant biotechnology product represents a major risk to be factored by companies into the R&D process, with such factoring affecting, and probably reducing, total investment decisions Diverting funds away from R&D could be especially critical to the survival of smaller DBCs which, unlike corporate seed suppliers, do not have seed revenues to offset short-term losses.

In some respects, regulation could be less an institutional barrier itself than a consequence of the barrier just discussed—poor knowledge base. Only further research can alleviate this lack and reverse the regulatory uncertainty it creates.

Property Rights

As discussed earlier, proprietary protection is critical to maintaining investment in research, especially commercially sponsored research. High costs for R&D and regulatory approval of products favor patenting because a company wants to protect its investment. Are there intellectual property issues that are barriers to developing plant agricultural research?

The structure of the plant protection system does not seem to be a barrier to commercial development (36)78), but rather an idiosyncrasy adding complexity to management of plant intellectual property. Some sentiment exists that patent and related issues are overblown (36,78), especially compared to regulatory issues (36). Choosing the type of protection to seek is characterized as a basic business decision (36). For example, there are advantages and disadvantages of securing protection of sexually and asexually reproduced plant varieties by obtaining a utility patent through 35 U.S.C. §101 rather than PPA or PVPA. Utility patents for plants provide somewhat greater protection (49,60) and lower nominal cost (60), and the holder of a utility patent can exclude others from using the patented variety to develop new varieties. A Certificate of Plant Variety Protection, however, affords 18 years of protection, whereas the life of a utility patent is 17 years. In the case of many agriculture companies, especially large firms, formal protection is not generally a part of their corporate milieu; rather they rely on trade secrets (ch. 6).

Although the domestic structure of plant intellectual property probably does not hinder commercialization, a lack of international harmony for plant protection is a potential barrier, especially considering the global economy in which the agricultural sector operates (31,36,47,78). Additionally, calls for patent extension for agri-biotechnology products (similar to the situation for pharmaceuticals) have been made. In light of the present regulatory uncertainty just described, some parties believe patent extension, based on the period a product is under regulatory review, would compensate companies and stimulate them to undertake higher risk research ventures. Analyses of international patent issues, how a type of protection is chosen by a company, and patent term extension will be analyzed in a forthcoming report on New ***Developments in Biotechnology: Patenting Life,***

Personnel Needs

Adequate numbers of trained personnel in a variety of disciplines are necessary for successful commercialization of U.S. plant agricultural biotechnology, and the demand remains substantially unmet (5,68). A 1985 survey found that companies seeking plant scientists cited shortages in plant molecular biologists who had solid education and training in plant science (as opposed to individuals who cross over from animal or microbial systems), plant tissue culture experts, and plant geneticists or breeders with expertise within vitro technologies (50). In other words, industry cited shortages in just about every area. These personnel shortages are not limited to the private sector, since industry draws its talent from universities. What measures could solve this problem?

The Federal role in funding education and training is crucial. Industry support—at universities or private institutions and in-house programs—is also important. Equally important is adequate research funding. Personnel needs are self-driven; if enough money is available to support research, then individuals will be drawn to the field. **Research funding drives the process, ensuring an adequate supply of trained personnel for universities, government, and industry.**

THE FUTURE OF AGRICULTURAL RESEARCH

The U.S. agricultural research enterprise is an evolving system. In addition to the three impacts just described, the changing global market for agricultural products affected and continues to affect agri-biotechnology research. In the late 1970s and early 1980s, the goal of increasing agricultural production drove public policy and the agricultural research agendas of both the public and private sectors. Today, however, the goal of U.S. agricultural research is increasingly focused on farming profitability.

In a recent survey, most Americans said that research into genetic engineering should be continued (98). Americans support and encourage a range of agri-biotechnology applications, such as disease-resistant crops, frost-resistant crops, and more effective pesticides (98). Given this popular support and these high expectations, what is the long-term outlook for U.S. investment in plant biotechnology research?

Increased Federal attention to agricultural research seems to be the most urgent need. In 1939, approximately 80 percent of federally sponsored research was for agriculture, while in 1985, agricultural research comprised less than 2 percent of Federal research expenditures. USDA, the largest Federal sponsor, is allocated only 5.2 percent of total Federal research funds, and only 1.4 percent of USDA's budget is used for research. Given the potential return on investment in agricultural research, the present spending pattern might be too low for priority research areas that have the ability to enhance and ensure the future competitiveness and profitability of U.S. agriculture (83). In particular, more fundamental research on plant applications is needed than on animal applications, because basic knowledge about plants is less (68). While recognizing the present climate of fiscal restraint, both public and private interests express the conviction that funding should be reallocated from other activities to agriculture, not reallocated within agriculture (95). Furthermore, increased integration between the basic biological sciences and applied agricultural research is paramount.

Agri-biotechnology research performed in the private sector has different long-term objectives from public sector research. What is the proper division of labor between the diverse interests? Balance needs to be found between molecular biology and traditional breeding private and public interests, and applied and basic research. While recent research agendas and interests of each sector have overlapped rather extensively, the public sector can no longer rely on the private sector to perform substantial basic research. The private sector, troubled by public sector usurpation, must also recognize the traditional responsibilities and constraints (including the broad and specific "public good" mandate) of the public sector. Applied research is an important component of the public agricultural research tradition—necessary to fill gaps left by industry, explore novel applications, and keep the government abreast of developments in the field. Accordingly, to strike and maintain a balance, agri-biotechnology research performed by both sectors will need careful management so that its research benefits the public and enhances the competitiveness of the U.S. agricultural industry.

At present, scientific, legal, economic, and political forces have seemingly converged to accelerate the rate of evolution and the direction of U.S. agricultural R&D. Yet change in the system is not novel, and adopting a siege mentality would be counterproductive (90). Serious new issues have been raised, but the embryonic nature of the agricultural biotechnology industry complicates the assessment of long-term effects. Continued examination and private and public support for long-range planning seem prudent.

ISSUES AND OPTIONS FOR CONGRESSIONAL ACTION

Three policy issues related specifically to applications of biotechnology to plant agriculture were identified during the course of this study. The first concerns possible congressional actions regarding research funding. The second involves regulating products of plant biotechnology, and the third concerns the impact of intellectual property protection of plants on germplasm exchange.

Associated with each policy issue are several options for congressional action. The options are not, for the most part, mutually exclusive, nor is the order in which the options are presented indicative of their priority.

ISSUE 1: Is Federal funding of research in plant biotechnology adequate?

Option 1.1: Take no action.

Congress could conclude that current Federal spending for plant agricultural research is adequate. Continuing the present level of funding, however, could result in a static agricultural sector that is unable to respond to future economic, technological, and scientific needs—both domestic and international. Knowledge in the plant sciences would continue to remain in short supply, limiting commercialization even further.

If Federal spending remains the same, the reduced role for public research could result in a slower rate of technological progress.

Option 1.2: Increase spending.

Congress could determine that present spending for agricultural research is insufficient. If Congress increases agricultural research funding, U.S. preeminence in this sector would probably continue, Increased expenditures for training would ensure an adequate supply of personnel for both universities and industry.

Option 1.3: Decrease spending.

The U.S. agricultural sector has added a surplus to the U.S. trade account every year since 1960, Underlying this success has been research support—with an annual rate of return for investment in agricultural research in the range of 33 to 66 percent.

If Congress determines that Federal investment in plant biotechnology is excessive, it could decrease allocations for this sector. Decreased funding for agricultural research would result in diminished returns that would undermine the agricultural economy.

Option 1.4: Reallocate existing resources.

Should Congress conclude that present funding levels are adequate or, because of fiscal constraints, must remain the same, then it could direct that Federal resources be reallocated.

Congress could increase the Competitive Grants Program at USDA at the expense of formula funding for land-grant institutions. Increasing dollars for peer-reviewed, competitive-based grants could bean effective mechanism to ensure that Federal investment in basic research is being well spent. However, historically, the nature of federally sponsored agricultural research has been applied. This fact, combined with a decentralized structure that includes local agricultural experiment stations and extension services, provides a unique national capacity to identify and solve local or regional problems. Reallocating resources away from formula-based funding would diminish the important role that even the smallest, poorest funded land-grant universities play.

Likewise, Congress could decrease spending for competitive grants within USDA or other agencies, such as NSF. In general, competitive research funding is directed toward basic research. Because the database for plant sciences is sparse, decreasing awards that foster excellence in this area could hinder rapid progress in plant biotechnology.

Option 1.5: Direct increases in State funding at State Agricultural Experiment Stations through the Cooperative State Research Service.

To increase total spending or offset Federal reductions, Congress could require States to increase their contributions to agricultural research through the Cooperative State Research Service at State Agricultural Experiment Stations. If increased State spending were to result in an overall increase for agricultural research, then continued development should occur.

ISSUE 2: Agricultural applications of biotechnology will increase significantly over the next several yearn Is the statutory and regulatory structure governing environmental applications of plant biotechnology adequate?

Option 2.1: Take no action.

Congress could take no action if it determines that the present regulatory structure provides adequate review to ensure environmental safety and public health, or that experience with the existing structure has been insufficient to ascertain its adequacy.

If Congress takes no action, the Coordinated Framework for the Regulation of Biotechnology (51 F.R. 23301) will continue to direct regulation of plant biotechnological products.

Option 2.2:Direct the Office of Science and Technology Policy (OSTP) to report on the implementation of the Coordinated Framework.

Congress could direct OSTP to evaluate, or specifically commission an independent analysis of, the process by which plant agricultural applications have been handled by regulatory authorities. A comprehensive review of the timeliness and efficiency of regulatory review, resolution of competing agency jurisdictions, scientific knowledge gained through field testing, actions of State and local regulation, community involvement, and consequences of field testing on environmental safety and public health could demonstrate whether the present regulatory framework best serves all interested parties.

Option 2.3: Relax regulatory constraints.

If regulatory requirements are judged excessive, Congress could direct executive authorities to relax regulations. The existing USDA regulatory authority for plant biotechnology includes the Federal Plant Pest Act (7 U.S.C. 150aa-150jj), the Plant Quarantine Act (7 U.S.C. 151-164, 166, 167), the Federal Noxious Weed Act (7 U.S.C. 2801 ***et seq.),*** the Federal Seed Act (7 U.S.C. 551 ***et seq.),*** and the Plant Variety Protection Act (7 U.S.C. 2321 ***et seq.)*** (51 F.R. 23339). Modifications that remove restrictions would make regulations for some applications more consistent with the regulation of nonengineered cultivars.

Less stringent regulation of environmental applications of genetically engineered plants might decrease costs associated with experimental field testing and increase investment in research. However, if planned introductions in the future (in contrast with those now contemplated or likely) define new risks, then reevaluating relaxed regulatory requirements could be necessary.

Option 2.4: Preempt State and local regulation of agricultural applications of biotechnology.

Increased State and local interest in regulating biotechnology exists. If Federal regulation of biotechnology is deemed adequate, Congress could enact a statute that preempts State and local regulation on this issue.

Uniform authority could remove some present regulatory uncertainty, streamline the process, and decrease delays in field testing. If Congress preempts such regulation, however, local concerns might receive less attention. Federal preemption could also hinder cooperative regulatory efforts between Federal and State agencies that are presently in place, e.g. the Animal Plant Health Inspection Service's regulation of genetically engineered organisms or products under the Plant Pest Act.

Option 2.5: Direct the Secretary of Agriculture to report how USDA is complying with National Environmental Policy Act requirements (NEPA) in its regulation of genetically engineered plants.

The statutory mission of USDA is to assist the development of agriculture and husbandry in the United States. NEPA requires all Federal agencies to consider the environmental impact of activities funded with Federal dollars.

If Congress determines that a conflict between NEPA requirements and the statutory responsibilities of USDA exists, then Congress could amend the mission of USDA to explicitly include environmental protection.

ISSUE 3: Does intellectual property protection of plants in the United States ensure adequate germplasm exchange?

Option 3.1: Take no action.

Congress could conclude that the present intellectual property structure for plant protection does not interfere with germplasm exchange. If Congress takes no action, inventors would continue to seek protection through the avenue they deem most appropriate or advantageous. Germplasm exchange would continue on an ad hoc basis.

Option 3.2: Direct the Secretary of Agriculture to report on the impact that plant protection has on germplasm exchange.

Congress could direct the Secretary of Agriculture to report on the impact that proprietary interests in plants has on germplasm exchange. To date, any information on the issue is anecdotal. Because all interested parties agree that free exchange of germplasm is necessary to continue progress in plant biotechnology, a comprehensive analysis examining trends in plant protection and germplasm exchange could reveal that a problem exists, that no problem exists, or could direct attention to potential problems.

SUMMARY AND CONCLUSIONS

The largest industry in the United States, agriculture is one of the most efficient and productive sectors in the country's economy. Agriculture contributes to approximately 20 percent of the gross national product, and employs more than 1 in 5 Americans. Increasingly, however, problems beset the U.S. agricultural economy. Research alone cannot solve all of the problems, but can significantly alleviate them if resources are available. Historically, the returns on Federal R&D in this sector have been high, so efforts to provide relief through agricultural research could yield powerful results.

Both public and private sector agricultural research endeavors are in a state of flux. Several factors have converged to affect U.S. investment decisions in such research, including the discovery of the new biotechniques, intellectual property rights and plants, and the funding source for plant agricultural biotechnology research.

Biotechnological innovation in plants spans a spectrum of applications, New techniques and new uses continue to arise. The new technologies can potentially accelerate the rate, precision, reliability, and scope of improvements beyond that possible through traditional plant breeding, while also reducing costs. Some have expressed concern, however, that biotechnology has led to private sector-, proprietary-dominated research efforts. others point out that biotechnology has afforded unique contributions to agricultural research and created positive economic effects. Biotechnology's effect on the balance of manpower between traditional plant breeders and molecular geneticists is seemingly reaching equilibrium.

Plant property developments have influenced agri-biotechnology research profoundly. Intellectual property protection of plants has stimulated interest and investment in plant research. However, increased plant protection activities have led to concerns about free-flowing exchange of germplasm. Such exchange is necessary to continued advances in plant breeding and biotechnology.

The U.S. agricultural research enterprise is lodged partly in the public sector and partly in the private sector. Each has different agendas and purposes. Understandably, the perceptions of proper roles, research priorities, and investment decisions clash. The issue of balance—formula funding v. competitive grants, private v. public, basic v. applied, traditional plant breeding v. molecular biology-seems foremost. Spending patterns by the public sector should be responsible and sensitive to broad public benefit. Industry can serve as an advocate for public agri-biotechnology research and as a funding source for research to enhance US. competitiveness. Adequate research funding also pulls in interested and qualified manpower to the agricultural research system.

The commercial profile of the plant agricultural sector does not appear to have changed appreciably since an earlier OTA report. Achieving widespread success, however, will require expansion of the plant science knowledge base, Lack of fundamental knowledge about plants and plant systems is probably the rate-limiting barrier to complete commercialization of plant biotechnology research. Regulatory uncertainty stands as the second major barrier and looms as potentially the most serious. Crop agriculture is particularly sensitive to regulatory delay—a one month lapse can result in a company missing the planting season and, thus, an entire year of development. In some measure, regulation itself could be less an institutional barrier than one arising from a poor fundamental knowledge base. Intellectual property issues do not appear to hinder commercialization, although patent term extension to compensate for regulatory delays might stimulate companies to undertake higher risk ventures.

Increased Federal and popular attention to agricultural research seems to be the most urgent need. Given the potential return for agricultural research, the present level of expenditures might be too low to ensure the preeminent role that guarantees U.S. agriculture vitality and profitability. While recognizing the present climate of fiscal restraint, proposals to reallocate already scarce agricultural resources to meet unmet needs disturb both commercial and public interests. In particular, USDA funding for fundamental research on plants is required to a greater extent than animal basic research. Furthermore, increased integration between the basic biological sciences and applied agricultural research is paramount.

As scientific, legal, economic, and political forces continue to direct U.S. investment in agricultural research, including plant biotechnology, ongoing examination and long-range planning seem prudent.

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