Chapter 1

Summary, Policy Issues, and Options for Congressional Action

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SUMMARY

Biotechnology can change the way we live. It has already provided, and promises to provide, many products never before available, as well as greater quantities of products now in short supply. Some products produced by biotechnology will be less expensive and safer to use than those now produced by other means. The potential of biotechnology to improve the Nation's health, food supply, and the quality of the environment leads logically to questions about the adequacy of current funding levels.

This report, the fourth in a series on new developments in biotechnology, analyzes the current level of support for biotechnology by the Federal Government, by State and local governments, and by the private sector. The report is titled "U.S. Investment in Biotechnology;" investment indicates expectation that the expenditures will result in significant benefits to society. Investment is treated broadly in this report to encompass financial resources, human resources, and industrial policies.

Any analysis, however, is confounded by wide variation in the definitions used by various sectors to describe biotechnology, and in the methods used to account for that investment. As a consequence, figures on expenditures are approximate, and the scope of investment cannot be determined precisely. It is important to look beyond the numbers to the scale and diversity of efforts underway within the United States to support research in biotechnology and its various applications. In this report, **biotechnology is broadly defined to include any technique that uses living organisms (or parts of organisms) to make or modify products, to improve plants or animals, or to develop microorganisms for specific use. This report focuses on "new biotechnology" (e.g., recombinant DNA techniques, cell fusion, and novel bioprocessing techniques) rather than "old biotechnology" (e.g., use of microorganisms for brewing and baking or selective breeding in agriculture and animal husbandry).**

Several conclusions are apparent about the nature of U.S. investment in biotechnology.

First, in some areas, the investment level is insufficient to meet the premise suggested by current work in the area. In particular, progress in such areas as agricultural biotechnology and biological approaches to waste disposal is hindered by inadequate investment by the public and private sectors. In both fields, technical barriers exist because of incomplete knowledge of basic processes involving plants, micro-organisms, and microbial ecology.

Second, the regulatory process is often perceived to be a significant obstacle to commercial development of some biotechnology-related products. Whether the perceptions are due to ambiguity, unresponsiveness, extreme caution, or outright bias, confusing regulatory mechanisms are seen by industry officials as a major impediment to the acquisition of knowledge and an obstacle to the economic success of future products. On the other hand, industry officials agree that reasonable and well designed regulations are necessary to ensure the public health and safety to the environment.

Third, the rate of biotechnology commercialization and the factors affecting that rate vary among industrial sectors. Policy issues relevant to the application of biotechnology to human therapeutics, for example, differ from those relevant to plant agriculture or chemicals.

How Much Does the United States Spend on Biotechnology?

Twelve Federal agencies and one cross agency program spent roughly $2.7 billion in fiscal year 1987 to support research and development in biotechnology-related areas (see table l-l). The National Institutes of Health (NIH) contribute by far the largest share of that support, approximately $2.3 billion. Significant investment

Table 1-1 .—Federal Support for Biotechnology Research, 1985-87 (current dollars in thousands)

Agency	FY 1985	FY 1986	FY 1987
National Institutes of Health:			
Basic	1,208,229	1,202,094	1,388,337
Applied	638,916	678,003	887,614
Total	1,847,145	1,880,097	2,275,951
Department of Defense:			
Basic	44,100	51,600	60,800
Applied	48,500	49,000	58,000
Total	92,600	100,600	118,800
National Science Foundation	81,570	84,072	93,800
Department of Energy:			
Basic	45,500	45,000	50,100
Applied	9,600	10,900	11,300
Total	55,100	55,900	61,400
USDA Cooperative State Research Service	*48,000*	46,000	49,000
USDA Agricultural Research Service	*24,500*	27,000	35,000
Agency for international Development:			
Broad definition	NA*	46,854	43,756
Narrow definition	NA	14,332	6,082
National Aeronautics and Space Administration	NA	6,400	7,200
Veterans Administration	5,400	6,365	9,400
Environmental Protection Agency.	3,000	3,400	5,666
National Bureau of Standards	850	3,300	3,300
Food and Drug Administration	3,000	4,700	5,800
National Oceanic and Atmospheric Administration.	2,144	2,215	2,680
Small Business Innovation Research**	12,033	12,000	NA

*NA: Not available.
**SBIR dollars are apart of the total spending reported by the above agencies. They should not be added onto total spending
SOURCE: Office of Technology Assessment, 1988.

is also being made by the Department of Defense, $119 million; the National Science Foundation, $93.8 million; and by the Department of Energy, $61.4 million. The Department of Agriculture expects to fund some $84 million in biotechnology research, divided between the Cooperative State Research Service and the Agricultural Research Service.

Federal support of biotechnology research and development has increased minimally every year since 1984. Although one reason for these increases may be its political attractiveness to agency officials, a more likely explanation is that biotechnology comprises a set of tools that have become fully integrated into the life sciences.

Some 33 States are actively engaged in some form of promotion of biotechnology research and development. These efforts are seen as a means to achieve academic excellence in their colleges and universities or as a path to economic development, or both. **State investment totaled $147 million in fiscal year 1987 (l/16th the Federal investment),** with three States—New Jersey, New York, and Pennsylvania—making up more than half of that amount. The States employ various funding mechanisms to reach their goals, including issuance of bonds, direct legislative appropriations, allocation of State lottery funds to biotechnology, and mandatory industry and government matching funds.

With the oldest State program, that of North Carolina, only in its sixth year, it is too early to judge the success of State efforts. The only available measures of success are indirect ones, namely, the size of the budget, the number of biotechnology companies within a State's borders, and the extent of involvement by universities and private industry. Although long-term, stable funding runs counter to the pattern of State investment, it is vital in the area of biotechnology. State programs with strong support from their governors appear to hold an advantage, as do those that can manage to avoid fiscal duress, severe unemployment, and educational insufficiencies. States that have an existing base of strong research universities hold the greatest advantage.

The commercialization of biotechnology by U.S. industry remains healthy and competitive. OTA identified 403 American companies dedicated to biotechnology, and 70 established corporations with significant investments in biotechnology. Combined, U.S. industry is spending an estimated $1.5 billion to $2.0 billion annually in biotechnology research and development.

Because biotechnology has become an essential tool for many industries, there is no such entity as "the biotechnology industry. " Rather, it is a tool employed by several industrial sectors, each with its own advantages and obstacles in the race to market. Human health care, primarily therapeutics and diagnostics, continues to be the focus of most R&D investments, with chemicals ranking second and agriculture third as fields of application for industrial biotechnology.

Strategic alliances between large corporations and smaller, dedicated biotechnology companies are increasing and are seen as a sign of financial strength by investors. Instability in the financial markets may accentuate the dependence of many smaller firms on large, established corporations. Most large corporations continue to rely on outside sources of innovation, either a smaller firm or a university scientist, with these collaborations benefiting both parties. However, the development of in-house expertise in biotechnology is occurring rapidly in major U.S. corporations.

Training' and Employment

The number of jobs in biotechnology has grown rapidly in the past decade. **A 1987 OTA survey of both dedicated biotechnology companies and large established corporations in the United States yielded an estimate of 35,900 jobs in the field, of which 18,600 are for scientists and engineers.** Nevertheless, despite employment growth in recent years, biotechnology is not expected to become a major industrial employer.

Although the supply of specialists in biotechnology appears adequate to meet current demand, shortages in particular areas will occur from time to time. Shortages in such emerging areas as protein engineering have occurred but were largely unavoidable. Anticipated shortages of bioprocess engineers have not yet developed, although the problem could worsen as more biotechnology products reach the later stages of commercialization. Demand for expertise in plant and animal tissue culture and protein chemistry may be outstripping supply, and a growing need for persons to assess the risks of engineered organisms released into the environment has led to a shortage of microbial ecologists.

The mix of personnel at biotechnology companies is changing as production and quality control become more important. The 1987 OTA survey of biotechnology companies found that Ph.D. scientists represent 20 percent of total personnel and 28 percent of scientific personnel. A 1983 survey had found that 43 percent of R&D personnel possessed Ph.D.s. This shift has created more opportunities for biologists and biochemists at the master's and bachelor's degree levels, and will be providing room for those with 2-year associate of applied science degrees.

Molecular biologists and immunologists constitute about a third of the research workers in biotechnology. For the most part, companies see an

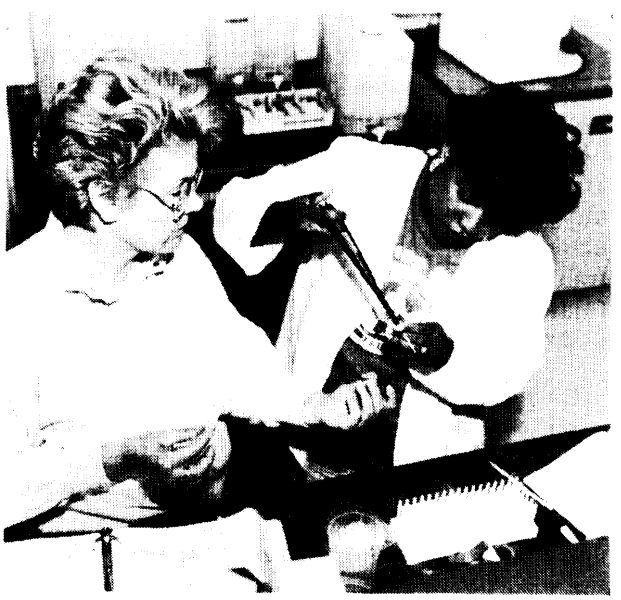

Photo credit: Center for Biotechnology, State University of New York, Stony Brook

Recombinant DNA and other new biological techniques are becoming well integrated into science education and training, from high schools to postdoctoral activities. In the workshop shown here, honors-level high school biology teachers are learning the techniques needed to set up DNA laboratories in their schools.

ample supply of scientists trained in molecular biology, biochemistry, cell biology, and immunology as a result of the traditionally strong support for those fields by the National Institutes of Health.

The NIH, by far the largest Federal source of fellowships and training grants, is also the largest supporter of such training for biotechnology. NIH estimates that $70 to $80 million of its training funds support graduate students working in areas either directly or indirectly related to biotechnology, approximately 6,000 students. At the same time, the share of NIH's research budget devoted to training has shrunk from 18 percent in 1971 to a low of less than 4 percent in 1987.

The National Science Foundation sponsors roughly 150 predoctoral fellowships, totaling about $8 million, in the biological and biomedical sciences. Only 20 fellows are funded at the postdoctoral level; these are all in plant biology and environmental sciences, at a total cost of $2.2 million. Other Federal agencies, notably the Department of Agriculture and the National Oceanic and Atmospheric Administration, support varying smaller numbers of students in areas related to biotechnology.

Based on a 1984 survey, biotechnology companies provide between $8 million and $24 million for training grants and scholarships. Industry funding is estimated to account for about 10 to 20 percent of all money for biotechnology training programs. Combined with the contributions made by industry to the research and salaries of trainees at research universities, industry provides financial assistance to about 20 percent of biotechnology trainees.

Colleges and universities have responded fairly rapidly to advances in biotechnology, by creating a range of new programs in biotechnology training and education. OTA has identified 60 such programs at 49 different U.S. colleges and universities. About three-fourths of these programs are based at State institutions.

Seventeen States reported funding university and college training programs in biotechnology. But complexities in accounting procedures and disbursement of such funds mean that few can provide exact dollar figures. For those that did report spending on specific programs, the figures for fiscal year 1987 ranged from a high of $1.3 million in Georgia to a low of $40,000 in Pennsylvania.

Campus-Industry Collaboration

Collaboration between industry and academia has always played an important role in biotechnology research. The industrial contribution to academic research is approximately four to five times greater in biotechnology than in other fields; per dollar invested, industrially supported university research in biotechnology generates four times as many patent applications as does company sponsorship of other research on campus. Nearly half of biotechnology companies support university-based research. Although small compared to the contribution made by the Federal Government, that support has grown by an average of 8.5 percent annually in the first half of the decade.

The nature of this commitment appears to be changing. Few biotechnology companies are planning to invest large sums over long periods for undirected research, as was done in the early 1980s by Monsanto at Washington University. An increasing number of cooperative arrangements represent consulting and contract research rather than long-term partnerships.

The debate over the impact of such collaboration on academic science remains unresolved. With the exception of isolated studies, little evidence exists to either substantiate or refute the claims that such cooperative efforts are undermining the university's mission and independence. As this debate continues, two tradeoffs bear watching:

- whether losses to science or to university values that result from increases in the level of secrecy in universities are offset by net additions to knowledge that result from infusion of industry funds into university laboratories; and
- whether shifts in the direction of the university research agenda toward more applied and commercially relevant projects have benefits for human health and economic growth that far outweigh the risks to basic research.

Collaborative efforts in biotechnology pose specific problems for each group of participants. A recent survey found that faculty receiving industry funds are much more likely than other biotechnology faculty to report that their research has resulted in trade secrets and that commercial considerations have influenced the choice of research projects. In another study, 40 percent of faculty with industrial support reported that their collaboration resulted in unreasonable delays in publication.

For industry, the major issue is whether such collaboration will prove fruitful and hasten the development of new products and processes. The nature of the agreement—specifically, who negotiates the contract and how property rights are assigned—plays an important role in the process and is, therefore, a major concern for companies entering into such agreements.

Added to those uncertainties is the great variation among collaborative agreements. Despite those variations, universities can take several steps when negotiating collaborative agreements to maximize the benefits to all parties and minimize potential risks. Those steps include specifying the scope of the agreement (the research area to be supported and the commitment expected from faculty); maintaining control over the selection, methodology, and review of the research to be undertaken; detailing the sponsor's responsibilities; and spelling out in advance guidelines on proprietary information, publication requirements, patent rights, and income. Apart from continued funding of the academic research that often sets the stage for such collaboration, the mechanics of Federal monitoring of such relationships are not without problems.

Any funding source has the potential to shape the research agenda and influence those who carry out the work. A history of Federal programs, dating from the Merrill Act of 1862 that established the land grant colleges, indicates how universities can be shaped by outside forces. While many early fears about the influence of industrial sponsorship of biotechnology research in university laboratories have not been borne out, the situation warrants monitoring. There remains sufficient concern about the long-term effects of such funds on research agendas, secrecy, conflict of interest, and student education.

Opportunities for Development

There is tremendous variation in the way that States and the Federal Government define and account for biotechnology spending. Also, there is no single model by which industry funds research in the field, nor is there a common approach to the carrying out of commercial developments of biotechnology products. At the same time, each sector affords significant opportunities to foster growth in the field.

At the Federal Level

The activities of the NIH determine to a large extent the nature of Federal support for biotechnology. In recent years the White House and others have increasingly pressured NIH to expand its mission and provide support for more applied research.

In 1986, an NIH committee began to draft guidelines that would permit companies unprecedented access to NIH resources. The guidelines, written in response to the Technology Transfer Act of 1986 (Public Law 99-502), give companies exclusive licensing rights to the fruits of government-sponsored research and encourage scientists to seek commercial applications for their work. This opening of the laboratory doors to commercial application offers great promise to the biotechnology industry, which has long relied on work conducted by NIH scientists.

Although the NIH investment in biotechnology dwarfs that of other agencies, opportunities to foster growth abound throughout the Federal Government. Other agencies, such as the National Science Foundation, the National Aeronautics and Space Administration, the Department of Energy, and the National Oceanic and Atmospheric Administration, fund basic and applied research in biotechnology. Agencies with diverse missions, such as the Departments of Defense and Agriculture, and those with regulatory missions, such as the Food and Drug Administration and the Environmental Protection Agency, fund biotechnology research relevant to their mandate.

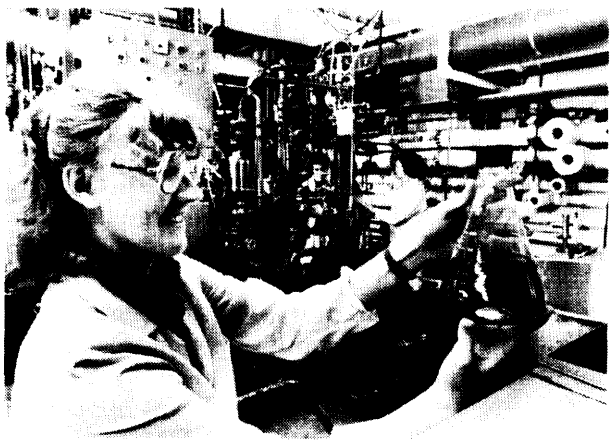

Photo credit: Marvin Lewiton

Undergraduate students in MIT's Bioseparations Research Laboratory, funded in part by the National Science Foundation and the National Institutes of Health.

Finally, agencies traditionally viewed as service oriented, such as the Veterans Administration, the Agency for International Development, and the National Bureau of Standards, fund biotechnology research relevant to their service roles. The National Bureau of Standards is a partner in a joint venture with the University of Maryland and Montgomery County, MD, to develop a national resource for biotechnology-related measurement research. A plan developed at the direction of the Senate Commerce, Science, and Transportation Committee estimated that measurement needs will add as much as 25 percent to the costs of biotechnology products, and the Bureau is devoting more than 2 percent of its budget to generic applied and basic research in this area.

The Small Business Innovation Research (SBIR) program has invested more than $36 million in various biotechnology companies since it first awarded grants in 1983. In fact, biotechnology is the leading recipient of SBIR funds, which are derived from a percentage of the budget of every Federal agency that spends at least $100 million on extramural research. SBIR invests more in biotechnology than in information processing and medical instrumentation.

Federal agencies report higher levels of support for applied work in biotechnology in fiscal years 1985, 1986, and 1987, than in 1984. Yet applied research support as a percentage of total R&D support has declined (in constant dollars) across the Federal research budget in the past 5 years. **It is not clear, therefore, whether an actual increase in support for applied biotechnology has occurred or whether agencies have become more proficient at describing work as applied and accounting for expenditures in those areas.**

By itself, greater support does not translate directly into successful ventures. NSF's Engineering Research Centers program expects to devote a growing share of a budget, which could reach $50 million in fiscal year 1988, to biotechnology-related work. Yet the effectiveness of the program has not been proven, and several factors could impede its progress. These factors include the reliance in funding decisions on scientific merit over other relevant criteria, inadequate coordination by Federal officials with State programs and the possibility of competing initiatives, and the lack of clearly defined evaluation and monitoring criteria.

Because Federal agencies seek an array of applications from biotechnology research, a certain amount of redundancy among supported programs is inevitable and probably healthy. At the same time, the goals of various agencies might at times be better met by increased cooperation among agencies wishing to pool their resources on common projects.

At the State Level

States have different expectations about their return on biotechnology investments, Some spend money to strengthen faculties so that universities can better attract private business to the State. Others offer direct incentives, including facilities and tax advantages, to attract small firms. Regardless of approach, successful programs rely on a strong academic and research base, sufficient local venture capital, and an unusually vigorous interaction among researchers, manufacturers and users, and State authorities.

Successful State programs in biotechnology build on previous efforts to attract high technology industries. Thus, it is not surprising that California and Massachusetts lead the nation in the share of biotechnology companies within their

Table 1-2.—State Allocations for Biotechnology R&D, Training, and Facilities

State	FY 86	FY 87
Arizona	$1,170,000	$1,540,000
Arkansas	757,173	800,000
California	2,500,000	2,500,000
Colorado	500,000	500,000
Connecticut	665,000	1,100,000
Florida	5,050,000	7,050,000
Georgia	2,600,000	3,000,000
Idaho	438,800	450,000
Illinois	4,500,000	5,000,000
Indiana	4,000,000	1,029,904
Iowa	500,000	3,750,000
Kansas	162,000	172,000
Kentucky	908,500	896,600
Louisiana	670,000	NA
Maryland	2,600,000	3,900,000
Massachusetts	485,000	935,000
Michigan	6,000,000	4,000,000
Minnesota	1,032,000	1,100,000
Missouri	1,500,000	3,700,000
New Hampshire	150,000	450,000
New Jersey	10,000,000	35.690.000'
New York	34,300,000*	*
North Carolina	6,500,000	6,900,000
North Dakota	1,643,090	1,601,783
Ohio	2,194,787	50,000
Oklahoma	1,584,000	1,542,000
Oregon	350,000	360,000
Pennsylvania	2,848,824	18,035,494'
Tennessee	NA	800,000
Utah	110,000	500,000
Vermont	NA	300,000
Virginia	1,500,000	1,750,000
Wisconsin	190,000	418,000

NA: Not available
"Indicates multi-year appropriation

SOURCE. Office of Technology Assessment, 1986

boundaries, with 27 percent and 13 percent, respectively. (See table l-2 for levels of investment in all States.)

An NSF program begun in 1978 to ensure greater geographical distribution of research awards has proven to be a springboard for biotechnology efforts in Vermont, North Dakota, Montana, Kentucky, and Oklahoma. While it is too early to assess the extent to which NSF's EPSCoR (Experimental Program to Stimulate Competitive Research) funds will help other States gain a foothold in the field, it is clear that several States had such a purpose in mind when they entered the program.

Most States are not aiming only to woo existing firms from other States. Instead, they have turned to nurturing in-State start-up companies in the hope that they will benefit from the industrial growth of those companies. And, as more companies seek sites for manufacturing facilities, States that could not provide unattractive environment for R&D facilities may be able to compete for the manufacturing facility. Regardless of the approach taken, States will remain dependent on Federal research support to universities to achieve their goals in biotechnology. Those contributions must be tied to the existing economic and academic base within each State.

Although some States may not be able to maintain current high levels of support for biotechnology, sustained commitments are vital for long-term success. Unlike the changes that have come about from growth in other high-tech areas, strategic investments in biotechnology promise to transform a State's entire economy, not just increase its work force temporarily or add to its industrial base.

At the Commercial Level

The boom in biotechnology company formation occurred from 1980 to 1984. During those years, approximately 60 percent of current companies were created, with nearly 70 new firms begun in 1981 alone. Consolidation within the industry and the predominance of a few firms have slowed the formation of new firms; nevertheless, the amount of money invested by larger, more diversified corporations continues to grow.

The range of companies commercializing biotechnology encompasses many traditional industrial sectors. They include pharmaceuticals, plant and animal agriculture, chemicals, energy, and waste management. Table 1-3 lists the primary emphases of biotechnology R&D of dedicated biotechnology companies and large, diversified corporations. Human therapeutics is the primary focus of both groups.

Each sector commercializing biotechnology faces different financial markets, public markets, regulatory requirements, patent issues, personnel needs, and problems in attaining product commercialization. As the tools of biotechnology become integrated into each sector, the paths to commercialization more closely resemble those historically taken for more conventional products.

Table 1-3.—Areas of Primary R&D Focus by Biotechnology Companies

Research area	Dedicated biotech companies #(%)	Large, established companies #(%)
Human therapeutics	63 (21%)	14 (26%)
Diagnostics	52 (18%)	6 (1 1%)
Chemicals	20 (7%)	11 (21%)
Plant agriculture	24 (8%)	7 (13%)
Animal agriculture	19 (6%)	4 (8%)
Reagents	34 (12%)	2 (4%)
Waste disposal/treatment	3 (1%)	1 (2%)
Equipment	12 (4%)	1 (2%)
Cell culture	5 (2%)	1 (2%)
Diversified	13 (4%)	6 (11%)
Other	31 (18%)	o (o%)
Total	296 (100%)	53 (loo%)

SOURCE Off Ice of Technology Assessment, 1988

More than in any other high-technology industry, commercial biotechnology expects R&D to generate revenues. The R&D budget for dedicated biotechnology companies surveyed by OTA averages $4 million per firm, or more than 40 percent of anticipated revenues. For large, established companies investing in biotechnology, the annual R&D budget for biotechnology averages $11 million, a figure that represents one-fifth of their total R&D expenditures. Although nearly every major corporation investing in biotechnology spends some of its R&D budget in house, 83 percent also spend some of their budgets on research conducted by outside firms or by universities.

To date, U.S. dedicated biotechnology companies have raised over $4 billion from private investors, according to one estimate. Yet 80 percent of that investment has been made in 10 companies. Investment in health care applications accounts for 75 percent of all investment. Agricultural applications have received only 16 percent of the total investment.

Dedicated biotechnology companies finance their research in two ways—through equity investments and collaborative ventures. If uncertain financial markets prevail, flexibility in access to equity may become restricted, resulting in an increase in joint ventures with larger more established firms. Venture capital and private equity have been the mainstay of support for start-up companies through 1987. As companies mature, however, they turn to public offerings. OTA found a decreased dependence on private investments, a doubling of U.S. equity holders, and a 10-fold increase in public stock offerings in maturing companies over a typical 5-year period. Dedicated biotechnology firms focusing on therapeutics are more likely to be publicly held than those in other fields, although several agricultural biotechnology firms issued an initial public offering in 1987 as they sought cash to bring their products to market.

Although equity investments also may come from individuals or financial institutions, corporate financing is the fastest-growing type of support. Historically, equity investments by large firms tend to be passive, giving the larger firm the chance to keep abreast of new developments. When these investments do lead to research contracts and product licensing agreements, the larger firm often handles final development, licensing approval, manufacturing and marketing, while the dedicated firm retains patent rights and receives royalties for the sale of the product.

Most industrial alliances occur between U.S. companies rather than between U.S. and foreign firms. Although collaborations with foreign companies may provide dedicated biotechnology firms with better access to international markets, there is a legitimate concern that such alliances could reduce future revenues and growth for U.S. firms. The most common foreign collaboration, when it does occur, is with Japanese firms, overwhelmingly in the application of biotechnology to human health care.

Barriers to Development

The growing concern that U.S. trade policy toward high-technology goods may be compromising national security poses a potential threat to the growth of biotechnology exports. Proponents of tighter controls argue that easing restrictions would give the Soviet Union easier access to Western technology. In the case of biotechnology, some fear that unrestrained exports would enhance the ability of other nations to produce biological warfare agents. On the other hand, opponents argue that strict controls will hamper economic competitiveness. A technical advisory committee within the Department of Commerce was formed in 1985 to address the question of biotechnology exports, but committee efforts to date have been marginal.

Photo credit: Monsanto

Genetically engineered tomato plants are shown being planted by researchers at a Monsanto-1 eased farm **in** Jersey County, IL.

The second major factor that could hamper commercialization of biotechnology is regulatory uncertainty. Biotechnology faces a much different and more stringent regulatory environment than do many other high technology industries because, among other factors, it is used by highly regulated industries, such as food and drugs. This environment promises to raise the cost of R&D and, thus, the amount of investment needed to market a product. One issue is whether a product produced using biotechnology will result in higher costs for regulatory review than similar products made using traditional methods. This issue will be resolved differently depending on whether the product is a pharmaceutical, an engineered organism, or a plant.

Other potential barriers to commercialization will also affect investment. With patent protection of biotechnology products a major unresolved issue, many companies have pursued trade secrecy as a short term and more certain strategy to assure protection of their technology. This strategy is not their optimal choice. With respect to antitrust issues, OTA was unable to find any aspect of the problem that could be considered unique to biotechnology companies. The impact on biotechnology of the Tax Reform Act of 1986 (Public Law 99-514) is not clear. Although some tax specialists believe that the revised incentives may affect the distribution of investment, they do not expect them to shrink the total amount of money available. At the same time, the repeal of the investment tax credit is expected to increase dramatically the tax rates in research-related areas. That rise is likely to have a long-term negative impact on biotechnology companies.

A Closer Look at Three Sectors

This report examines three areas of research and development in biotechnology; plant agriculture, human therapeutics, and hazardous waste

management. Each is of legislative and regulatory interest to the Federal Government, and each presents a different set of issues for debate. Differences in the state-of-the-art, levels and proportions of public and private support, the effects of regulation, and the degree of commercialization in each area illustrate the necessity of viewing biotechnology as a diversified set of tools affecting a variety of sectors.

Biotechnology as applied to the development of human therapeutics represents an area where there has been substantial Federal support of basic research. As a result, the knowledge base is vast and growing, the commercial aspects enticing, and the regulatory regime similar to that applied to more traditional approaches of drug design and manufacturing. In contrast, plant biotechnology faces a smaller knowledge base due to lower levels of Federal support for basic research in the plant sciences. The commercial applications in the field are less developed, although potentially highly profitable, and the regulatory framework new and evolving. The third case study, biotechnology as applied to hazardous waste management, represents an area of minimum R&D investment by both the public and private sectors. As a result, the knowledge base is small and large scale application nearly nonexistent. Applications of biotechnology in this field tend to be driven by regulation.

Human Therapeutics

Biotechnology has become an integral part of research in the pharmaceutical industry, where the emphasis has already begun to move away from technology development and toward clinical applications. Applications of biotechnology to the development of human therapeutics enjoys a level of public and private funding for R&D that greatly exceeds that in any other sector. Such high levels of support stem from expectations that recombinant DNA and hybridoma technologies will bring about the development of products never before available in the quantities necessary for therapeutic applications. Contributions thus far include the production of naturally occurring human proteins through the use of recombinant DNA technology and the production of monoclinal antibodies from rodent and human hybridoma cell lines; others are expected from the available technologies for making proteins function more efficiently and for creating proteins that do not exist in nature.

Photo credit: Centocor

Industry scientists sterilize vials for monoclinal antibodies.

In the face of such promise, it is noteworthy that only seven human therapeutics using biotechnology have been approved for marketing in the United States. There are more than 400 biotechnology-based human therapeutics in some stage of clinical trials, comprising less than 2 percent of the 25,000 active applications for investigational new drugs. Nevertheless, of the 20 FDA approvals of new human therapeutics in 1986, four were products of recombinant DNA or hybridoma technology, This high approval rate of biotechnology products is one reason why industry analysts project billions of dollars in worldwide sales of therapeutics made from the new technologies, and should help to sustain or increase the level of public and private investment.

Six major factors will influence the rate of progress in the development of human therapeutics:

- availability of funds for research;
- support of personnel;
- regulation of products made using biotechnology;
- protection of intellectual property;
- access to information generated by research; and
- gaps in basic research.

Plant Agriculture

A critical industry in the United States, agriculture forms a large portion of this country's economy. Research contributes significantly to its success, with an annual rate of return on investment estimated at between 30 and 50 percent. Biotechnology is expected to play a major role in strengthening this important part of the nation's economy. Its tools have the potential to modify plants to resist insects and disease, grow in harsh environments, provide their own nitrogen fertilizer, or be more nutritious. The newer technologies can potentially lower costs and accelerate the rate, precision, reliability, and scope of improvements beyond that possible by traditional plant breeding. But success in this field is by no means assured. Many barriers must be overcome for US, agricultural products to remain competitive in world markets.

Of all the problems facing agricultural research, the most pressing is the need for increased Federal support. Only 1.4 percent of the Department of Agriculture's budget is devoted to research. In part, the advent of genetic engineering and related biotechniques has, itself, altered the shape and scope of U.S. agricultural research investment decisions. In particular, the emerging technologies present fundamental challenges and opportunities for the public component of U.S. agricultural research. Widespread commercialization of plant biotechnology depends on breakthroughs in many technical areas that can come only through cooperation with public universities, economic incentives from government, and a favorable regulatory environment. The Federal Government also plays a major role in ensuring an adequate supply of trained personnel.

Basic science advocates charge that the USDA-led system has not been on the cutting edge of science, and has focused research primarily on methods for increasing yield. Other critics have argued that the advent of the biotechnologies has led to private sector, proprietary-dominated research efforts. Others point out that increased private sector research investments have uniquely contributed to the fundamental knowledge base and resulted in a positive economic impact.

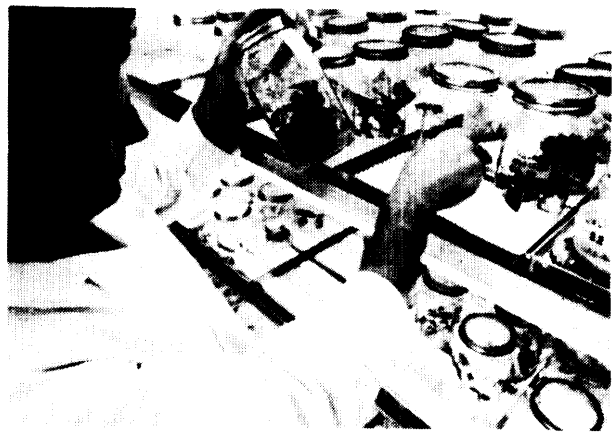

Photo credit: Calgene

Cell and tissue culture methods are used to regenerate plant cells containing foreign genes into whole plants.

Biotechnology's impact on the direction of agricultural research has also raised issues about proprietary interests, such as the exchange of plant breeding materials.

Hazardous Waste Management

Waste cleanup is a substantial and growing industry. But the application of biotechnology to waste disposal is still largely experimental, and the investment is small compared with efforts in pharmaceuticals and agriculture. Its potential remains undeveloped due to a variety of technical, institutional, economic, and perceptual barriers, And, more so than in any other industry studied by OTA, the research agenda for waste disposal and management is driven by regulation. The influence of the regulatory regime affects, to a large degree, the extent to which biotechnological applications have been studied, Regulation shapes the field of waste disposal and, thus, provides the impetus for efforts to develop new methods of pollution control. Yet fears of regulatory barriers are discouraging researchers from investigating genetic engineering as a way to discover potentially beneficial organisms.

The Environmental Protection Agency is the lead agency in conducting research and development in waste disposal. But EPA's current investment in R&D in biotechnology is not sufficient to overcome a number of technical barriers in the near

future. There is also a widespread feeling that EPA is biased against biological approaches to waste disposal and unwilling to support approaches involving biotechnology. The field lacks credibility because biological techniques were oversold during the 1970s. In addition, many biological approaches take longer than incineration or excavation and are avoided because of a desire to address the problem quickly.

Funding appears to be insufficient and comparatively unstable. The in-house research EPA funds is of high quality, but it is at a relatively low level. At the same time, reports from individual companies lack credibility due to the potential conflict of interest inherent in any company-sponsored research. The Federal Government must take the lead in addressing critical research areas and establishing clearly defined cleanup standards.

Because of these factors, small start-up biotechnology firms usually cannot afford the high financial risk required to achieve progress in the field. The large initial investment needed to develop the appropriate technology, as well as the necessary knowledge base, is another obstacle.

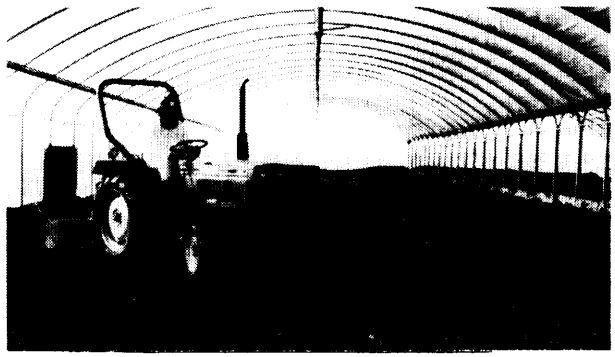

Photo credit.' Ecova Corp.

Daily tilling of soil provides oxygen to naturally occurring microbes, enabling them to remediate hydrocarbon-contaminated soil in an enclosed, solid-phase soil treatment facility. Current applications of biotechnology to waste management rely on naturally occurring microbes; the application of genetic engineering to this field remains some years away.

Finally, public acceptance is required to implement biotechnological approaches to waste disposal. The generic fear of genetically engineered organisms may be compounded by the difficulty of containing the waste to be disposed.

POLICY ISSUES AND OPTIONS FOR CONGRESSIONAL ACTION

Ten policy issues relevant to U.S. investment in biotechnology were identified during the course of this study. They are:

- Federal funding for biotechnology research;
- balancing support for basic and applied research and development;
- interagency cooperation in support of biotechnology;
- information needs and reporting requirements;
- training biotechnology personnel;
- monitoring university-industry relationships in biotechnology;
- Federal support of State programs in biotechnology;
- providing financial incentives for private investment in commercial biotechnology;
- providing direct support for start-up and scale-up in commercial biotechnology; and
- Federal controls on the export of biotechnology products and processes.

Associated with each policy area are several issues that Congress might consider, ranging from taking no action to making major changes. Some of the options involve direct legislative action. Others are oriented to the actions of the executive branch but involve congressional oversight or direction. The order in which the issues and options are presented should not imply their priority. The options provided for each issue are not, for the most part, mutually exclusive: adopting one does not necessarily disqualify others in the same category or within another category; however, changes in one area could have repercussions in others. **Finally, and of critical importance, many of the issues are more germane to certain sectors, such as human therapeutics, plant biotechnology or hazardous waste management In those cases, specific issues and options are presented at the end of chapters 9, 10, and 11.**

ISSUE 1: Should current levels of Federal funding for biotechnology research and development be altered?

An issue central to the findings of this report pertains to the adequacy of Federal support for R&D relevant to biotechnology. There are no objective and reliable measures for determining whether current Federal support for biotechnology R&D is sufficient. Clearly, intensive and sustained Federal investment in applications of biotechnology to the life sciences has been transformed into commercial products in some industries much faster than in others. Commercial applications are more advanced in areas such as human therapeutics, diagnostics, and chemicals than in plant and animal agriculture, or bioengineering for waste degradation. In some cases, the slow progress is due to insufficient funds for basic research; in other cases, potential products are simply not being developed because industry does not consider the biotechnology product or process sufficiently better (either functionally or economically) than those that already exist. Furthermore, excessive regulatory burdens or public perceptions associated with applications of recombinant DNA research can be more important factors than underfunding in some biotechnology applications, most notably in plant agriculture.

Option 1.1: Take no action.

Congress may conclude that Federal levels of investment in R&D over recent years have adequately supported the forward integration of biotechnology into many sectors, suggesting steady levels of support as the best approach. The continuance of existing funding patterns, however, will perpetuate current disparities in research emphases.

The current focus of biotechnology application on human health care products is due, in part, to the steady and high levels of funding for biomedical research. However, research applicable to medical biotechnology has moved only recently from technology development into new clinical applications; without Federal funding increases, this transition could be more difficult.

Maintaining the existing funding level for biotechnology research targeted to agriculture could result in a static agricultural sector that is unable to respond to future economic, technological, and scientific needs—both domestically and internationally. Basic knowledge in the plant sciences, for example, would continue to remain in short supply. The barrier to commercialization created by this lack of knowledge would increase. Inadequate funding could also slow some areas of research to help alleviate surpluses, provide new options for the small farmer, result in better products, and make farm practices more environmentally sound.

Biotechnology for waste management has suffered in recent years from a variety of funding and institutional barriers. Its development is in a relative state of infancy compared with that of biotechnology in pharmaceuticals and agriculture. Without sufficient funds, adequate efficacy and efficiency demonstrations will not be carried out, and EPA is not likely to develop sufficient in-house professional expertise for the assessment and regulation of bioremediation techniques.

Particularly underdeveloped areas of biotechnology research could remain stagnant in the absence of additional funds. These areas include: the exploitation of marine organisms to obtain new sources of potential pharmaceuticals, industrial chemicals, and materials; and the development of new biotechnological applications, such as conversion of biomass to fuel and biological sensors for use in measurement devices and bioreactors.

Option **1.2:** *Decrease existing budgets.*

Due to current fiscal constraints, Congress may conclude that it is necessary to cut Federal funding of biotechnology research. Such a decision is more likely to be a consequence of overall reductions in R&D budgets, of which biotechnology would be a part. Reductions in Federal support for biotechnology could slow the transfer of basic research results to applied areas and would require greater private investments in basic research.

Congress could determine that funding of health-related applications of biotechnology is disproportionately high, and reduce funds in these areas. A targeted reduction of research funds for biotechnology applications to human health could have undesirable consequences for non-medical

sectors, however, because advances in biotechnology continue to emerge from NIH-funded research that have immediate applications to agriculture, marine biology, the use of micro-organisms in waste management, and many other fields.

Some areas of research, currently underfunded, would suffer disproportionately. For example, Federal support for biotechnology R&D in waste treatment is so minimal now that decreases will further retard new developments. If Congress determines that Federal investment in plant biotechnology is excessive, it could decrease allocations for this sector. However, decreased funding for agricultural research and training would result.

Option 1.3: Increase existing budgets.

Congress could conclude that because of its social, economic, and strategic importance, the rapid development of biotechnology and its transfer into many sectors warrants increased Federal R&D support. Increases could expand the knowledge base necessary for applied research and development and could result in more rapid commercialization of biotechnology in some fields.

Funding increases in the application of biotechnology to basic and applied research relevant to human health might be aimed at some of the important bottlenecks, including research in protein structure and function, protein engineering, the role of natural chemical modifications of proteins in protein stability and function, and development of novel delivery systems for protein drugs. Additional support in many of these areas should continue to yield generic applications--contributing to uses in the pharmaceutical industry as well as chemical, agricultural, and other diversified industries.

Congress could determine that present spending for agricultural research is insufficient. If Congress increases agricultural research funding, plant biotechnology is likely to benefit. The basic science base in the plant sciences is seriously deficient.

Congress could provide additional funds for EPA to develop innovative waste cleanup technologies, particularly those derived from biotechnology. Without increased funds, EPA will continue to emphasize funding of risk assessment studies on micro-organisms containing recombinant DNA, while other high priority projects continue to be supported at relatively low levels.

Increased funds for the application of biotechnology to renewable biomass resources, and for the exploitation of marine biotechnology, currently funded primarily by DOE and NOAA, respectively, should enhance the United States' role in developing these novel uses.

Option 1.4: Reallocate existing funds.

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. Although the budgetary process works against centralized research planning, Congress could decide that pressing needs for advanced R&D in specific industrial sectors warrants a shift of emphasis in research support. This option, however, promotes a degree of instability in patterns of research support in that political and temporal influences could overly bias the National research agenda.

ISSUE 2: Are current emphases on basic v. applied and multidisciplinary research appropriate?

Anecdotal evidence suggests that the current system of research support in the U.S. sometimes fails to fill critical gaps in basic research related to biotechnology and development. Gaps could be filled through additional financial support for applied research, technology transfer, and increased Federal support for multidisciplinary research programs.

Option 2.1: *Direct Federal agencies to dedicate more of their budgets to applied and multidisciplinary research in biotechnology.*

This option would not necessarily require new funds but would direct agencies to identify areas of applied research in biotechnology in which awards could be made. Applied areas deserving increased funding could be identified by committees of peers comprised of government, academic, and industrial scientists. In addition, areas of research that require multidisciplinary involvement could receive higher levels of support.

For example, at the NIH, support for individual investigator-directed, basic research projects in

disciplines underlying medical biotechnology–such as cell biology, immunology, virology, neurobiology, structural biology, and genetics---could be redistributed to multidisciplinary programs involving researchers from several of these disciplines. possible mechanisms for implementing this approach might involve Congressional reallocation of single investigator awards to center grants (center grants are common in the categorical institutes but not in National Institute for General Medical Sciences). An alternate approach would require that NIH contribute to health-related multidisciplinary projects funded by other agencies, such as the NSF-administered Engineering Research Centers and Biological Centers Programs. Congress might also reallocate NIH funds to create centers and programs that have not moved as rapidly as desired with funds from individual agencies. Such a program is already in place, for example, to apply new methods in structural biology to AIDS vaccine development.

Historically, agricultural research has been applied. The applied nature of the land grant system, 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 role that even the smallest, poorest funded land-grant universities play. Congress could protect the applied orientation of agricultural research by maintaining strong formula-based funding at the expense of competitive research funding, which is directed towards basic research. Because the database for plant sciences is sparse, however, decreasing awards that foster excellence in basic research could hinder rapid progress in plant biotechnology.

To support more applied work applicable to hazardous waste management, Congress could direct EPA to devote more funds to applications research in demonstration and evaluation. Comparative data on the efficacy, economics, and environmental safety of biotechnical versus other methods is lacking. Additional efforts in testing and evaluation would significantly assist industry development, resolve issues relating to efficacy of specific techniques, and, along with regulatory changes, promote private sector investment.

Any effort to increase emphases on applied research carries the risk of harming the support base for basic science, the source of new ideas. Each agency needs to consider the balance of support between basic and applied work within its mission. Service-oriented agencies, such as the Agency for International Development and the Veterans Administration, report that they emphasize applied research, which best supports their mission. Recent efforts to support more applied and multidisciplinary research at the National Science Foundation indicate a shift in the historical mission of that agency. Such shifts are viewed with skepticism and encouragement, depending on the observer's outlook.

Option 2.2: Require agencies to report on the extent to which the goals of the Federal Technology Transfer Act of 1986 (Public Law 99-.502) *have been met.*

Under The Federal Technology Transfer Act of 1986, directors of government operated Federal laboratories may enter into collaborative R&D agreements with other Federal agencies, State and local governments, industrial organizations, and nonprofit organizations. Biotechnology is an area of research currently pursued in many Federal laboratories that could be more effectively shared with industry and universities through active compliance with Public Law 99-502. As one means of encouraging compliance with the intent of the law, Congress could request that agencies document the extent to which this has occurred within their laboratories.

ISSUE 3: Should there be more interagency cooperation in funding biotechnology R&D?

Some redundancy and duplication of effort is essential to a healthy research enterprise. However, more formal cooperation between agencies in areas of shared interest could facilitate more rapid advances in some areas of biotechnology lacking sufficient or focused support.

Option 3.1: Establish an interagency coordinating body to identify areas of research *that could be co-funded across agencies, address solutions to filling research needs, and develop strategies to promote technology transfer.*

Congress could conclude that this option would reduce some redundancy in Federal research ef-

forts in biotechnology and promote cost savings. This type of cooperation might best be implemented through across agency coordinating body that meets regularly to discuss shared areas of research interest in biotechnology. At present, such coordination is rare and informal.

Applications of biotechnology to human health enjoy the highest levels of Federal funding. The overall medical biotechnology research agenda is evolving from research funded almost exclusively by the National Institutes of Health, with additional contributions from the National Science Foundation, the Department of Defense, and the Department of Energy. A coordinated effort by these agencies is essential if unnecessary duplication is to be avoided and the technological gaps impeding medical applications of biotechnology are to be removed.

A recently formed cooperative effort in plant sciences was initiated by the Office of Science and Technology Policy. The Plant Science Initiative, to be co-funded by the National Science Foundation, the Environmental Protection Agency, and the Department of Agriculture, aims to address gaps in research areas of common interest to each agency.

Advances in the use of bioengineering in waste clean-up could benefit from this type of coordinated approach. For example, EPA, NIH, NSF, the Department of the Interior, the Department of Energy, and the Department of Defense have significant programs related to bioengineered waste cleanup technologies. An interagency coordinating group could identify major gaps in the research and work to prevent unnecessary duplication of efforts by Federal agencies.

ISSUE 4: Are information requirements for informed decisionmaking about Federal support of biotechnology R&D and training being met?

Currently, information about Federal support for biotechnology research and training is scattered and inconsistent. Systematic evaluation of total Federal spending and a direct comparison of spending in specific areas across multiple agencies are complicated by the definition of biotechnology each agency employs and by the method of accounting for expenditures.

Option 4.1: Direct Secretaries and Administrators to report regularly on biotechnology activities.

The Congress could conclude that strategically important areas, such as biotechnology, are important enough to the Nation's economic growth that a more systematic accounting of Federal investment in supportive research is warranted. Authorization Committees could direct individual agencies to develop more routine systems of accounting for spending in specific areas, such as biotechnology, so that overall trends and possible necessary actions can be identified. Some agencies, such as the National Science Foundation and the National Institutes of Health have already adopted such mechanisms. Regular and institutionalized reporting on levels of funding for research and training could promote a more coordinated approach to setting strategies for biotechnology development.

Option 4.2: Direct Secretaries and Administrators to agree upon a uniform definition of biotechnology.

The adoption of a uniform definition could resolve vagueness in future policy development and would allow for more direct comparisons of research support across agencies.

However, Congress could decide that in the absence of any comprehensive mechanism for affecting total Federal spending in biotechnology, there is no sound reason to request that all agencies funding and conducting biotechnology R&D adopt a uniform definition of biotechnology. Given the various and diverse missions of the agencies, flexibility in definition may be desirable. This argument might not apply to reasons to adopt uniform terminology for the purpose of regulation. Also, given the rapid advances in research, any definition would have to be flexible enough to accommodate new technologies or would soon be obsolete.

ISSUE S: Are Federal efforts in training and education for biotechnology sufficient?

Federal funds, directly and indirectly, support a significant amount of training and education for biotechnology. Most of these funds are directed at research rather than training, but contribute to training nonetheless.

Option 5.1: Take no action.

Training and education for biotechnology in the United States is strong, successful, and well supported. For the most part, personnel needs for the industry are being met. While shortages have been difficult to predict in advance, they have been short lasting when they have occurred. By and large, the current system is working well, though additional support in specific areas could pay off significantly. If Congress takes no action, the United States can expect to continue to enjoy high quality personnel in the biological sciences, but certain needs may not be met and the fit between personnel needs and availability may not be optimal.

Option 5.2: Require Federal agencies to direct more funds for training.

While NIH, USDA, NSF, and other Federal agencies provide substantial research funds, which contribute indirectly to training, training grants and fellowships are less well funded and have declined in recent years. In molecular biology, competitive training grants have effectively encouraged university departments to establish coherent training programs and enable money from faculty research grants to be used for research rather than salaries. Training grants in particular areas of possible need, such as bioprocess engineering, plant molecular biology, microbial ***ecology, and*** protein crystallography, could be given special consideration.

Option 5.3: Increase funds for the National Science Foundation or other Federal agencies to provide equipment for biotechnology education and training programs.

Equipment and instrumentation for biotechnology training and research is expensive. Almost every program contacted by OTA reported unmet needs for equipment and facilities. Direct Federal support for R&D equipment and physical plant has been declining, leaving many universities with outmoded equipment. Direct support for instrumentation in biotechnology could provide many programs with much needed equipment, enabling them to train students on state-of-the-art equipment used by industry. Such funds may also encourage researchers from related areas, such as chemistry and engineering, to collaborate in biotechnology research.

Option 5.4: Establish programs to foster the interdisciplinary education needed for most applications of biotechnology.

Peer-reviewed, individual investigator initiated grants provide the bulk of funding for basic research but may be biased against the interdisciplinary nature of many research projects in biotechnology. Interdisciplinary programs could foster the interaction among various fields needed to improve research and training for biotechnology and promote technology transfer across fields and industrial sectors. Congress could encourage agencies to more actively support programs that foster multidisciplinary training in areas related to biotechnology.

Option 5.5: Request the National Academy of Sciences to assess comprehensively future personnel needs in biotechnology.

Given the long time needed to prepare individuals for careers in biotechnology, it is important at both the national and the individual level to be able to anticipate personnel needs several years into the future. The Committee on National Needs for Biomedical and Behavioral Research Personnel of the Institute of Medicine has twice systematically investigated personnel needs in biotechnology by surveying U.S. biotechnology companies. These surveys provide important information on recruitment difficulties faced by biotechnology companies, assist policy makers in setting appropriate funding levels, and enable students to make more informed career choices. Though the Committee was able to make these studies in 1983 and 1985, funds were not available for a similar study in 1987. The National Academy of Sciences could update and expand this work by seeking additional information from the U.S. Department of Agriculture, the Environmental Protection Agency, and the National Institutes of Health on medical, agricultural, environmental, and other personnel needs in biotechnology and the role of predoctoral versus postdoctoral support as it affects the pool of available biotechnology personnel.

Such personnel forecasts, however, depend on assumptions about gross national product, demographic trends, government policy decisions, technological innovation, foreign activities in the field, and other factors that cannot be known with certainty. Given the uncertainty of many of the

assumptions that must be considered in making forecasts about labor demand, making such forecasts may be futile. OTA has concluded in previous reports that predictions of shortages should be treated with skepticism. Market forces often significantly alleviate any shortages that do develop. It may be that accurate forecasts of future needs are neither possible nor necessary.

ISSUE 6: Should Congress set guidelines for university policies on industry-sponsored research?

Industrial sponsorship of university-based biotechnology research has become a widespread and generally accepted phenomenon over the past five years. These relationships have provided additional resources for R&D and training in university laboratories, and appear to have facilitated technology transfer into industry. Some of the early fears concerning the potential for skewing the research agenda toward more applied work, increased secrecy among scientists, and negative influences on the educational process have not been realized. Yet there remains concern that if public funds for basic research decline, universities may become more reliant on private funds, possibly allowing some of these fears to be realized.

Option 6.1: Take no action.

Because there is little empirical evidence that university-industry relationships in biotechnology have had significant adverse effects, Congress may conclude that no action is necessary, Most universities whose faculty have entered into contractual agreements with industry have already developed institutional guidelines regulating such agreements. These agreements appear to be satisfactory to participating parties. In addition, most parties continue to be optimistic about the goals of these relationships and are more comfortable with them than they were 10 years ago. Congressional action might stifle interchange between academe and industry.

On the other hand, most Federal research dollars are spent on university campuses. Allowing individual institutions to self-police these relationships while continuing to receive Federal funds could diminish public accountability.

Option 6.2: Require Federal granting agencies to request that universities receiving Federal research money file guidelines for faculty-industry contracts as a condition of receipt of funds.

To ensure that Federal funds are not being used to support research that becomes overly secret or proprietary, Congress could direct agencies to require universities to submit guidelines regarding faculty consulting and contractual agreements. Most research universities have already developed such guidelines. Under this option, those that have not would be forced to do so. While this option would not guarantee that undue secrecy or conflict of interest would not occur, it would encourage universities to set clear policies regarding limits of acceptability for faculty-industry interactions. In addition, this option is consistent with requirements that universities file statements of assurance that other areas—such as protection of human and animal research subjects—are being monitored.

On the other hand, while this approach could raise the accountability level of universities and scientists receiving Federal funds, it could add a layer of bureaucracy to an already burdensome grants process.

Option 6.3: Ensure that a minimal level of facility and equipment needs are being met by public funds to decrease the potential for disproportionate university reliance on private funds,

Industrial sponsorship of research augments public funding, but contributes only partially to the unmet capital needs of universities. Congress could decide that in order to avoid the consequences of some universities relying disproportionately on industry for research funding, adequate levels of construction and equipment grants should be available through granting agencies. This option would not prohibit or discourage universities from seeking industrial funds but would free them from undue reliance on the private sector.

Some would argue, however, that the private sector should make a **larger** contribution to university research if it wants to reap its benefits. Increased public subsidies for university research will allow industry to make even less of a contribution than it already does.

ISSUE 7: Do State efforts in biotechnology need Federal assistance?

There are few mechanisms by which the Federal Government can properly assist State programs in biotechnology. Historically, those States receiving large percentages of Federal research dollars through their universities have held an advantage over those that have received less. In an effort to address distribution inequities, the National Science Foundation initiated the Experimental Program to Stimulate Competitive Research (EPSCoR) to assist States in the development of science and technology programs. The EPSCoR program has helped some States gain a foothold in biotechnology.

Option 7.1: *Take no action.*

Congress could conclude that Federal assistance for State efforts in biotechnology is unwarranted. The EPSCoR program has assisted those States with historically lower levels of Federal research support in developing new programs in biotechnology, as well as many other fields.

Option 7.2: *Direct the NSF to consider an extension of the time frame for EPSCoR grants.*

Under the provisions of the current EPSCoR program, qualifying States receive 5-year continuing grants for program development. At the end of the 5-year period, funding ends. Under other programs at NSF, such as the Engineering Research Centers and the Science and Technology Centers, grant recipients demonstrating outstanding achievements are eligible for a new 5-year grant at the end of the first five years. This is not the case in the EPSCoR program. Because it is likely to take longer than five years to establish a new program at the State level, EPSCoR recipients that can demonstrate progress should also be eligible for continued funding after five years. This would allow the stability necessary for States to build the support and infrastructure required for a successful program.

ISSUE 8: Should the Tax Reform Act of 1986 (Public Law 99=514) be amended to provide greater incentives and assistance for firms commercializing biotechnology?

Option 8.1: Take no action.

The tax measures of the Tax Reform Act could remain as they are. These provisions include: extension and reduction from 25 to 20 percent of the R&D tax credit; repeal of the investment tax credit for equipment investment; and abolition of the preferential treatment for capital gains. Due to current fiscal stress, Congress may determine that the provisions of the Tax Reform Act of 1986 are equitable. However, if as a result of some of these measures, the level of private investment in biotechnology is reduced, there will be a negative effect on the level of innovation. This will manifest itself in decreased equipment and capital investment.

Option 8.2: Make the R&D tax credit a permanent part of the U.S. Tax Code and increase it from 20 percent to its original 25 percent incremental rate.

The purpose of the tax credit is to provide an incentive to companies to increase their commitment to industrial R&D. The R&D tax credit was renewed when it expired in 1985. The credit will again expire at the end of 1988. At this time, Congress could grant the R&D tax credit permanent status. A permanent credit would reduce the uncertainty that exists for industrial R&D planners concerning the credit's future existence. In addition to permanent status, Congress could restore the credit to its original level of 25 percent. This was the level adopted in the 1981 Economic Recovery Tax Act (Public Law 97-34).

Option 8.3: Offer the R&D credit to start-up dedicated biotechnology companies.

The structure of the R&D credit currently provides a 20 percent credit for expenditures in excess of the average amount of R&D expenditures for the previous three years. The purpose of the incremental credit is to provide incentives to companies to increase research expenditures. Companies that do not have a 3-year expenditure base are not eligible for the R&D credit as it is currently structured.

Congress could offer a refundable credit to start-up companies in the year earned. A refundable tax credit would be more valuable to biotechnology start-ups in the year earned than a tax credit

carried forward to the years in which enough taxable income would be earned to take advantage of the credit.

Option 8.4: Make the basic research tax credit a permanent part of the U.S. tax code.

The basic research tax credit, an incentive included in the 1986 Tax Reform Act, encourages companies to increase spending on basic research at universities and other non profit research institutions. It is seen as a mechanism to encourage cooperative relationships between industry and universities. On contractual research, the credit equals 20 percent of the company's total contract research payments over a fixed base. A permanent credit of this sort would reduce future uncertainties associated with this tax incentive.

Option 8.5: Restore the preferential treatment of capital gains incurred under Research and Development Limited Partnerships (RDLPs).

Under the new tax law, capital gains are treated as ordinary income. The former treatment of capital gains attracted investors to RDLPs because the gains from the sale of a limited partnership were treated better than the dividends themselves. Because RDLPs represent a large portion of the investment in biotechnology, Congress could reinstate the preferential treatment of capital gains for investors in RDLPs. This would restore incentive for investors to pursue this investment option, thereby increasing private investment in the biotechnology industries.

ISSUE 9: Are Federal mechanisms for assisting biotechnology firms in obtaining the financing necessary for start-up and scale-up adequate?

To date, venture capital and private equity placement have been the mainstay of biotechnology start-ups. Nearly all dedicated biotechnology companies in existence have received venture capital. As firms mature, they turn to public offerings and corporate equity investment as sources of funding. There are inherent risks to overdependence on any of these sources. Venture capital sources may become restricted because of fluctuations in the economy. The risks of reliance on the public markets to finance scale-up and production may be too great for firms caught in a downturn in the market. To ensure the continued growth and maturation of biotechnology companies, Congress could decide that more aggressive action is needed to assist biotechnology companies in two critical stages—start-up and scale-up. Support of industrial innovation could, in part, finance areas of applied research and development not already supported through the Federal research agencies.

Option 9.1: Take no action.

Congress could decide that the growth of biotechnology companies has been a result of creative financing through available sources of capital. Congress could conclude that sufficient investment capital is available to commercialize biotechnology and the Federal Government need not intervene at this time.

Some have argued that traditional policy discouraging government subsidies for industrial innovation places the United States at a disadvantage compared to other industrial nations, which have targeted funds to support industrial biotechnology. Allowing the marketplace to remain the sole influence over the health of these industries may be detrimental in the long run.

Option 9.2: Direct the Small Business Administration to evaluate programs under existing authority that could provide a source of venture capital funding for small businesses, biotechnology included.

The Small Business Investment Act of 1958 authorized the Small Business Investment Company, or SBIC Program. SBICs are privately capitalized, owned, and managed investment firms that provide equity capital, long-term financing, and management counsel to new and expanding small business concerns. They are licensed and regulated by the Small Business Administration and can borrow funds from the Government on a long-term basis for reinvestment in small business. SBICs, however, have faced uncertain congressional funding and restricted access to capital markets. To insure continued availability of venture capital for biotechnology, the Small Business Administration, with proper authority, could form a quasi-governmental corporation that would raise money in the private sector to be used as a venture capital fund for start-ups. The SBA could

evaluate the success of the SBIC program and make recommendations for its improvement.

ISSUE 10: Is the current export control system as dictated by the Export Administration Regulations working efficiently in the approval of biotechnology products for export?

The Departments of Commerce and Defense each play important roles in the export control process. The DOC monitors the Commodities Control List (CCL) and the DoD monitors the Militarily Critical Technologies List. Each agency brings to the process a different philosophy on what export controls should accomplish. As more and more biotechnology products become available for export, there is some concern on the part of industry that these products will become caught between the interests of Commerce and Defense, or will become delayed due to administrative confusion about the required approval process for biotechnology products.

Option 10.1: Take no action.

Congress could determine that the current export control system as dictated by the Export Administration Regulations is working efficiently, and has achieved a sufficient balance between economic and national security interests. The 1985 amendments to the Export Administration Act (EAA) addressed several issues that were not covered in the original EAA. For example, foreign availability and decontrol were two items that were to be emphasized by the agencies. However, little progress in the reduction of the CCL has been made.

Maintaining the current CCL could adversely affect the U.S. position overseas because it is often viewed by U.S. and foreign industry as encompassing too many products and technologies, making it difficult to manage. Continued operations under the present system could hamper efforts to promote U.S. products abroad and penetrate valuable foreign markets. The final outcome could be migration of U.S. industries abroad to avoid U.S. export regulations.

Option 10.2: Congress could decide that the present export control system is adequate and could request that even greater controls be enacted.

Those in favor of greater controls are concerned that our national security would be compromised by reduction of the CCL and decontrol of goods even when foreign availability is documented. Once foreign availability is documented, decontrol can be withheld while negotiations are pursued with supplier countries. The result has been that few items have completed the procedures necessary for decontrol and removal from the CCL.

Congress could request that the agencies involved in the export control process maintain stricter control over exports. For the biotechnology and other high-technology industries, this could result in the loss of valuable overseas markets to foreign competitors in Western Europe and Japan, This may also provoke overseas migration of companies who do not want to be burdened with U.S. unilateral export controls.

Option 10.3: Direct the Secretary of Commerce to evaluate the efforts of the Biotechnology Technical Advisory Committee (TAC).

The Biotechnology TAC began in early 1985 to advise agencies involved in export control on technical matters and new developments in the biotechnology industries. The TAC can make recommendations to the Department of Commerce on items to be removed from the CCL. This mechanism of communication between the biotechnology industries and those in charge of export control policies is valuable to both parties. The TAC can give important technical information to the actors involved in controlling biotechnology exports. Thus far, however, the TAC has submitted recommendations of items to be decontrolled and has seen no results. Because the decontrol process is often held up for national security reasons, few items have been removed because of foreign availability. Congress could request the Department of Commerce to review the TAC, with the intent to develop recommendations for improved use of the TAC mechanism.