Chapter 6
Factors Affecting Commercialization and Innovation in Biotechnology

"No amount of R&D funding can overcome unresolvable bureaucratic obstacles to the testing and use of new biotechnology. ”

Frank E. Young
FDA Commissioner, 1987

"It's difficult to imagine how biotechnology could be 'controlled. ’ “

Robert Yuan
International Trade Administration
Department of Commerce
Sept. 15, 1987

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INTRODUCTION

Counting dollars spent on biotechnology research is only one way to measure the vigor of commercial biotechnology. Assessing industrial policy is just as useful. Although the concept of a U.S. industrial policy has been around since the New Deal, most recently it returned to the national agenda in 1983 as part of the presidential election campaign. Difficult to define under any circumstances, industrial policy as it relates to biotechnology is nonexistent. However, several factors comprising industrial policy, such as tax rules, antitrust law, trade and export policy, patent law, and the regulatory climate, can be discussed in terms of their effects on biotechnology. The following section describes policies, legal frameworks, and administrative laws affecting commercialization and innovation in biotechnology.

TRADE ISSUES

There is a growing concern in some sectors that pursuing a trade policy that promotes high-technology goods for export compromises our national security objectives. This conflict might impede the export of biotechnology products unless economic and national security interests become balanced. As U.S. biotechnology industries have expanded, attention has focused on international promotion and commercialization. Many believe that high-technology industries, such as those employing biotechnology, might contribute to our economic competitiveness and provide a partial remedy for our current deficit crisis.

However, several aspects of U.S. unilateral controls have the potential to put U S. biotechnology firms at a competitive disadvantage relative to those of the other members of the Coordinating Committee on Multilateral Export Controls (CoCom). Formed in 1949 to coordinate multilateral trade controls to Soviet bloc countries, CoCom has 16 member nations. Because the biotechnology industries are still developing, it is difficult to discern exactly how much of an effect these export controls and barriers to trade will actually have, reasons, The National Academy of Sciences (NAS) recently estimated that in 1985, export controls cost the U.S. economy approximately $9.3 billion (24). The debate is composed of proponents who believe that relaxing export controls would increase the accessibility of Western technology for the Soviets and opponents that believe excessive controls harm U.S. economic competitiveness and trade relations (5). In the case of biotechnology exports, some argue that unrestrained export will enhance the ability of other nations to produce biological warfare agents.

Export Controls

Export controls can impede export transactions. They restrict international technology transfer for national security, foreign policy, or short supply

Mechanisms of Control

Controls for biotechnology exports come primarily under the jurisdiction of the Food and Drug Administration (FDA), the Department of Commerce (DOC), and the Department of Defense (DoD). Different statutes may apply to the exportation of a biotechnology product—the FDA's Federal Food, Drug, and Cosmetics Act (FFDCA) and its Drug Export Amendments Act (Public Law 99-660), the DOC's Export Administration Act (EAA) (Public Law ***96-72)*** and its amendments, *and the* Export Administration Act Amendments of 1985 (EAAA) (Public Law 99-64). Other agencies, such as the U.S. Department of Agriculture (USDA) or the State Department, may be asked to review potential decisions, but have no direct regulatory power under these statutes.

FDA Approval

Since the passage of the Drug Export Amendments Act of 1986 (Public Law 99-660), FDA approval is no longer a necessary requirement for exportation of drugs and biological products. These amendments abolished the law requiring FDA approval prior to exporting, giving U.S. biotechnology companies greater **access to** the international market. Before this law was passed, the companies either licensed their technology to foreign manufacturers, established foreign manufacturing facilities, or lost the business abroad. The path has been cleared substantially, though the FDA still must approve the export request, and with few exceptions, the product can only be exported to those countries that are on a list of 21 countries specified in the Act and that have already approved the drug. Furthermore, the exporter must have a written agreement from each importer stating that the importer will not export the drug to any countries that do not appear on the list of 21 countries (15). The export license is subject to cancellation if the FDA finds that the company is not actively pursuing approval. (See ch. 9 for further discussion.)

DOC Oversight

DOC plays a large role in the export control process through its licensing system. Its activities in export control are guided by U.S. foreign policy, national security, or supply issues. In the case of biotechnology, attention will most likely be focused on exports perceived as threats to U.S. national security (15). The DOC follows the procedures contained in the 600-page Export Administration Regulations (24). Many products and technologies require only a general license, and need no application to be exported. Referral to the Commodity Control List (CCL) is necessary for a biotechnology company to determine whether it needs to apply for a validated license for its product, and if so, what type. The CCL is published by the DOC and administered by the DOC's Bureau of Export Administration. It divides goods and technologies into categories and also into geographic groups according to a country's level of control. Controlled commodities on the unclassified list are categorized into 10 groups; groups 7 and 9 pertain to biotechnology. Group 7 is primarily chemical compounds with a subgroup that includes DNA, culture media, pharmaceutical products, proteins, and nucleotides; group 9 includes microorganisms, viruses, bacteria, fungi, and protozoa.

If an item or technical data are included in one of the categories of the CCL and there is evidence that it is available abroad, it is necessary for the DOC's Office of Foreign Availability to conduct an assessment. If the item is available in sufficient quantities and is of comparable quality, the item is supposed to be decontrolled. However, if after a positive determination the President believes that decontrol will threaten national security objectives, a "national security override" maybe enacted (25). Attempts may then be made through negotiation to persuade the foreign sources to enact controls to eliminate the foreign availability (7). Once the determination is made, the results are published within 30 days in the *Federal Register* **(25).**

DoD Oversight

DoD oversees products and technologies that appear on the Militarily Critical Technologies List (MCTL). Unlike the CCL, the MCTL is not a control list; rather it provides a technical basis and guidance for DOC export decisions on technology and equipment that may be used in military systems (24,36). The unclassified MCTL contains four parts—arrays of know-how; keystone manufacturing, inspection and test equipment; keystone materials; and goods which could reveal know-how relevant to the U.S. military system (36). It includes biotechnology products that have dual-use status—products with both civilian and military applications. For example, bioreactors or high-capacity separating devices are dual-use technologies because, in addition to their positive applications, they can also be used to produce biological warfare agents (3). One of the categories with direct relevance to biotechnology covers know-how for recombinant DNA and bioprocessing technologies.

Due to the limited number of biotechnology products on the market at this time, it is difficult to predict how the DOC will interpret the sections of the MCTL relevant to biotechnology. In addition to its role in export controls, the DoD also has oversight in the patent law process. The Department is entitled to screen applications and can request the DOC to impose secrecy orders on

patents, causing them to become classified information.

Effects of Controls

Since the **1984** OTA report *Commercial Biotechnology: An International Analysis,* was published, there has been little substantive change in export controls and trade issues as they relate to biotechnology. However, with more products available, the DOC will be more taxed regarding licensing applications. According to some industry representatives, current export policies disregard the interests of biotechnology firms, and are not always administered consistently (12). The prevailing view in industrial circles concerned with export control in biotechnology is that the issues are worse now than they were before the 1985 Amendments were passed, Some suggest that the agencies involved are inadequately staffed and poorly trained to deal with the complexity presented by biotechnology and other high-technology areas.

The DOC underwent a reorganization after the passage of the EAAA. Issues of export control are now handled in a newly created entity of the DOC. The Bureau of Export Administration now has its own Under Secretary and is no longer housed under the International Trade Administration (ITA). The previous position of Export Administration raised conflict of interest questions because the ITA was involved with both the promotion and the control of exports. The new level of Export Administration gives more visibility to the export control issues.

The decontrol of technologies on the CCL has proved to be a contentious issue. If the DOC's Office of Foreign Availability conducts an assessment and determines that an item is available abroad, then that item is supposed to be decontrolled. A recent NAS study concluded that the technology decontrol process has not been carried out effectively. NAS attributed this to the lack of time constraints in the legislation and the excessive influence of the DoD. It was also recommended that the in-house technical and analytical expertise of the DOC be upgraded, particularly in the areas of high-technology products and processes (24).

However, the DOC has not been totally ignorant of industry needs. In 1986, DOC responded to criticisms that the controls were retarding West-West trade, by introducing a certified end user or "gold-card" status to approved, reliable companies in Japan and 14 European nations (24,7). These 2-year licenses speed up the export process by eliminating the need for repeated applications for export licenses to those buyers. Whether this provision is as useful to high-technology goods exporters as originally predicted remains to be seen.

In addition, under the direction of the DOC's Bureau of Export Administration, a Technical Advisory Committee (TAC) met in April of 1985 for the first time. Similar TACs exist to advise on issues in computer systems, electronic instrumentation, semiconductors, telecommunications, and transportation. The Biotechnology TAC includes both biotechnology industrialists and government representatives from the DOC, DoD, and State Department. Members are nominated to TAC and serve 4-year terms of office. They provide information and advice to participating agencies on technical matters, export regulations affecting biotechnology, issues of trade development as affected by the controls, worldwide availability, and new technological developments. However, the TAC was not set up to provide members of the biotechnology industries with information about the export control process (11). It is not clear that the goals of TAC have been met, particularly in the decontrol of items available abroad. At a September 1987 meeting of the TAC, members expressed some concern about the productivity of their efforts.

Due to expire in September of 1989, the EAA is again being discussed in Congress. The issue that remains is whether it is possible for Congress to formulate a policy that balances U.S. foreign policy and national security interests while pursuing national economic vitality. The outcome of this debate is important to the future success of the biotechnology industries, because they may be placed at a competitive disadvantage relative to nations without unilateral controls. **The economic potential of the biotechnology industries may never be realized if companies cannot comply with the procedures and restrictions associated with the Export Administration Regulations (12).** Under review are several

aspects of the legislative proposals that apply to biotechnology. These are:

- outlining the specific functions of the government agencies involved in the export control process, thereby clarifying the DoD's role;
- removing controls (licensing requirements) on low-technology items;
- developing and enforcing timelines for decontrolling items that have been found outside the United States by the DOC's Office of Foreign Availability; and
- reviewing the Commodity Control List with the intention of reducing its size (17).

Other Barriers

Other trade barriers also affect biotechnology products. Actual tariffs on products are rare. Nontariff barriers, defined as "any government intervention affecting competition between imported and domestic goods" (33), are most likely to present obstacles for U.S. biotechnology products abroad. The barriers to biotechnology transfer that were identified in the 1984 OTA report remain. These are standards and certification systems, subsidies, price regulation, and government procurement. All are methods to protect a product's domestic market.

REGULATORY CONCERNS

In a report prepared for the Environmental Protection Agency (8), market considerations were cited as dominant factors influencing industrial biotechnology R&D strategies. However, the status of governmental regulation can become a primary factor by affecting the cost, time to market, and especially the uncertainty of R&D. Thus, when regulation is untried in the marketplace, untested in the courts, or ambiguous in status and scope, the resulting set of uncertainties can become a dominant influence in selecting or rejecting an R&D objective and associated business strategies.

Multiple tensions among uncertainty, market potential, and the economic factors of production can affect research, production, and marketing decisions in many significant ways. Because the range of commercial opportunities for biotechnology is uncommonly wide, regulatory uncertainty could be a factor driving firms away from applications in areas of high uncertainty to those of lesser uncertainty.

Interviews with a number of senior executives in biotechnology firms revealed that a substantial majority of them see regulatory uncertainty as being among their most pressing problems, including specifically the increased cost of performing R&D and doing business generally. The General Accounting Office (GAO) has noted that regulatory requirements vary considerably by product type and by the agency charged with regulatory responsibilities. Each agency employs its own internally defined standards and procedures (32).

While the regulatory aspects of biotechnology are covered in *Field Testing Engineered Organisms: Genetic and Ecological Issues (34),* it is important to underscore the relationship of several of these to private R&D costs and investment in biotechnology. Analysis of a variety of reports and interviews with key individuals in and out of government leads to a major conclusion: from an industry perspective, regulatory uncertainty looms as a critical factor in the future of biotechnology. **It is likely that biotechnology faces a much different and more stringent regulatory environment than do many other components of**

Photo credit: Monsanto

Genetically engineered tomato plants are shown being planted by researchers at a Monsanto-based farm in Jersey County, Illinois.

high-technology industries, increasing the cost of R&D and the amount of total investment required. In addition, the regulatory framework encompasses several agencies, each with its own approach to approval. At present, uncertainties are being resolved and ambiguities identified. It is too early to assess the effects of regulation on commercialization of biotechnology.

The international features of biotechnology regulation will present additional uncertainties. Proposals to establish an international set of guidelines under the auspices of the Organization for Economic Cooperation and Development (OECD) have not been successful. Three U.N. organizations—the U.N. Industrial Development Organization, the World Health Organization, and the U.N. Environment Program—have launched a program to establish new safety guidelines for the infant biotechnology industry in the Third World. Minimum safety guidelines for biotechnology are intended for eventual adoption by *all* countries (19). Biotechnology firms are warily watching the unfolding of regulatory decisions in Europe, Japan, and the United States (38,28).

Industry representatives told OTA that biotechnology progress will be hindered unless the Federal Government pays a great deal more attention to the regulatory arena, especially to risk assessment activities and programs. Former EPA Administrator William Ruckelshaus has put this directly:

> The Administration must attach a high enough value to maintaining our worldwide lead in this technology to devote enough government resources to its regulation so that real public concerns about risks can be satisfied. And that level of attention has not yet been evident from this Administration (23).

Regulatory issues specific to applications of biotechnology in human therapeutics, plant agriculture, and waste use and pollution control are discussed in chapters 9, 10, and 11.

PATENTS AND INVESTMENT

When the Supreme Court addressed the issue of patenting living organisms in Diamond v. *Chakrabarty* in 1980, the potential profitability of biotechnology became apparent to scientists and investors. Since then, 6,000 biotechnology patents have been filed with the the U.S. Patent and Trademark Office (PTO) (37). The tangle of patents awaiting approval is one of the more difficult dilemmas facing the industry today as more and more products near the market. Already, patent battles are being fought over interleukin-2, tissue plasminogen activator, human growth hormone, hybridoma technology, alpha interferon, factor VIII, and use of dual monoclinal antibody sandwich immunoassay in diagnostic test kits. There is significant uncertainty about how the courts will interpret the claims for biotechnology patents. Companies receiving basic product patents are in court enforcing their rights against infringement or defending the patent grant in opposition or revocation proceedings. It is likely that patent litigation in biotechnology will increase given the complex web of partially overlapping patent claims, the high-value products, the problem of prior publication, and the fact that many companies are chasing the same products. Many companies are finding it essential to determine a product's patent position prior to marketing (2). Chapter 9 discusses some of the difficult patent issues facing the human therapeutics industry.

This report does not attempt to assess the complexities of these disputes. An upcoming OTA report on *Patenting Life* will address legal issues in greater detail. It is important to note, however, that patent uncertainty is a critical factor affecting commercialization in biotechnology. Companies face a battle on two fronts: domestic and international. The protection of U.S. patents abroad is currently being pursued by U.S. representatives of the General Agreement on Tariffs and Trade (31).

Investors watch the biotechnology patent battles and often react quickly to the latest legal decision. For example, in September 1986, Genentech's stock dropped 10.5 points following the

The patent awarded to Stanley Cohen and Herbert Boyer in 1980. This patent has since become Stanford University's top earning patent ($1.7 million annually).

United States Patent [19]

Cohen et al.

[11] 4,237,224

[45] Dec. 2, 1980

[54] PROCESS FOR PRODUCING BIOLOGICALLY FUNCTIONAL MOLECULAR CHIMERAS

[75] Inventors: Stanley N. Cohen, **Portola Valley; Herbert W.** Boyer, **Mill Valley,** both **of Calif.**

[73] **Assignee:** **Board** of Trustees of the Leland Stanford Jr. University, **Stanford, Cal if.**

[21] Appl. No.: 1,021

[22] Filed: Jan. 4, 1979

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 959,288, Nov. 9, 1978, which is a continuation-in-part of Ser. No. 687,430, May 17, 1976, abandoned, which is a continuation-in-part of Ser. No. 520,691, Nov. 4, 1974.

[51] Int. Cl.³ C12P 21/00

[52] U.S. Cl. ..... 435/68; 435/172; 435/231; 435/183; 435/317; 435/849; 435/820; 435/91; 435/207; 260/1 12.5 S; 260/27R; 435/212

[58] Field of Search ..... 195/1, 28 N, 28 R, 112, 195/78, 79; 435/68, 172, 231, 183

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Primary Examiner— **Alvin E. Tanenholtz**

Attorney, Agent, or **Firm--Bertram I. Rowland**

[57] ABSTRACT

Method and compositions are provided for replication and expression of exogenous genes in microorganisms. Plasmids or virus DNA are cleaved to provide linear DNA having **ligatable** termini to which is inserted a *gene* **having complementary** termini, to **provide a biologically functional replicon with a desired phenotypical property. The replicon is inserted into a microorganism cell** by **transformation.** Isolation of the transformants **provides cells for replication and expression of the DNA molecules present in the modified plasmid. The method provides a convenient and efficient way to introduce genetic capability into microorganisms for the production of nucleic acids and proteins, such as medically or commercially useful enzymes, which** may **have direct usefulness, or may find expression in the production of drugs, such as hormones, antibiotics, or the like, fixation of nitrogen, fermentation, utilization of specific feedstocks, or the like.**

14 Claims, No Drawings

SOURCE: **Office of Technology Licensing, Stanford University,**

news that Hoffman-La Roche had sued it for infringing a patent for human growth hormone. Genentech's stock rose the previous year when it sued Burroughs-Wellcome (PLC) for allegedly infringing a British patent on tissue plasminogen activator.

On average, DBCs have filed fewer biotechnology patent applications than larger, established firms—1.5 versus 10 applications in 1986. This is most likely due to a greater institutional capacity to file multiple patents in the larger, more diversified companies.

How the courts uphold issued patents, and interpret new ones, as well as how well U.S. companies are able to protect patents abroad, will be issues facing biotechnology forerunners in the next few years. Uncertainty over patent protection is likely to be costly and will undoubtedly influence the R&D strategy of many companies. In the short term, trade secrets are being sought as an alternative route for the protection of products. Eighty-five percent of the large corporations responding to the OTA survey indicated that they expect to pursue trade secrecy protection for biotechnology lines in addition to patent protection. While there is no time limit on trade secret protection, disclosure terminates protection. In addition, where parallel research is underway, there is a high likelihood of simultaneous invention, presenting a threat to trade secrecy. While biotechnology industrialists are skeptical about the value of trade secrecy versus patents, the former could bean option where inventions simply are not patentable because they fail to meet the statutory criteria of novelty, non obviousness, and utility. Trade secrecy is probably more likely to be employed for invented processes rather than for products (26). Ultimately, patent protection facilitates licensing transactions and is more desirable for many DBCs (22).

Patent and Trademark Office

At the PTO, the Biotechnology and Organic Chemistry group has experienced a turnover of and a difficulty in acquiring patent examiners with expertise in fields associated with biotechnology (see table 6-1). Under these circumstances, it is about 24 months, on the average, before processing of a biotechnology patent application is initiated. In contrast, 6 months is the average time that passes before examination of patent applications for conventional drugs begins (37). This time lag, along with an atmosphere of general uncertainty over patent rights, may cause companies developing biotechnology products to file many **more patents than are typical for conventional drugs.**

There are two reasons why government personnel reviewing drug marketing approval or patent applications become dissatisfied with their positions. First, the work tends to be repetitive and administrative, a disincentive for trained scientists used to more interesting and creative work. Second, these individuals are often capable of earning substantially higher salaries in the private sector. In a rapidly evolving technology such as biotechnology, the industrial regulatory affairs and legal offices (among others) can profit greatly from the "insider's view" of personnel trained at Federal agencies. **Federal incentive programs for trained scientists that will bring them to and keep them at these types of positions in government are vital to the impact of biotechnology on drug development, as well as to other major areas of applied biotechnology.** The PTO is currently undergoing a reorganization of those groups dealing with biotechnology products that is expected to reduce the time lag for patent approvals.

Table 6-1.— Biotechnology Staff and Workload Trends in the U.S. Patent and Trademark Office, 1985-88

	As of Jan. 1988	As of Jan. 1987	As of Jan. 1986	As of Jan. 1985
Examiners	42	32	30	30
Pending applications				
New (not yet acted on)	4,051	3,307	3,155	2,202
Tentatively rejected	2,472	1,879	2,173	1,529
Amended	384	651	445	172
Total	6,907	5,837	5,773	3,903
Total completed (granted or abandoned in previous year)	2,190	2,044	1,573	1,171
Approved applications (previous year)	887	816	712	556
Percent approved	40.5 "/0	40 "/0	45.30/0	47.5%

SOURCE Charles Van Horn, U S Patent and Trademark Off Ice, 1987

ANTITRUST CONSIDERATIONS

OTA was unable to identify antitrust law issues or difficulties unique to biotechnology. The larger debate on antitrust essentially concerns economic policy and high technology in the framework of global competition. However, as was suggested in an earlier OTA report (33), two issues should be raised with respect to biotechnology:

- whether U.S. antitrust law discourages or inhibits formation of R&D joint ventures, thereby retarding innovation and the competitiveness of U.S. firms in world markets; and
- whether U.S. antitrust law inhibits the legitimate exploitation via licensing arrangements of the technology created by R&D efforts.

American companies have traditionally avoided collaboration in R&D. The principle reasons seem to arise from the view that cooperation does not result in benefits, an unwillingness to share proprietary data and decisionmaking, and fears of private or government antitrust actions. But global competition and the rising costs of performing R&D are driving some major U.S. corporations to consider alternatives to internally generated and financed research projects. In biotechnology, a group of companies interested in forming a consortium to conduct research in protein engineering has met to develop plans and raise funds (18).

Since 1980, and especially since passage of the National Cooperative Research Act of 1984 (NCRA) (Public Law 98-462), research consortia have begun to proliferate in various industrial sectors, especially in microelectronics (14). Both the Departments of Commerce and Justice have promoted and encouraged the formation of research consortia to cope with foreign competition. However, the breadth and vagueness of the antitrust statutes, along with perceived ambiguity in the guidelines and business review procedures used by the Justice Department, have resulted in widely held beliefs that collaborative research organizations would be threatened by antitrust actions (27).

Despite underlying suspicion by industry, the Justice Department has never challenged a pure research joint venture under the antitrust law. Between 1950 and 1980, only three joint R&D ventures were challenged, and each involved significant collateral restrictions that were deemed to retard innovation (13). Further, no plaintiff has ever won an antitrust case against a member of a collective research effort (39).

The NCRA was aimed to reduce uncertainty and the level of risks associated with antitrust. It specifically removed the threat of treble damages and made it costly to file frivolous private antitrust actions. Further, NCRA makes it clear that a rule-of-reason analysis will be used to assess the competitive effects of any R&D joint venture. The rule-of-reason concept is important because it means that the licensing practices of an R&D joint venture cannot be automatically condemned under the so called *per se* illegal doctrine, but must be weighed in terms of competitive benefits and any adverse competitive effects. Only those practices found on balance to be anticompetitive could be subject to enforcement action or judicial decree.

Response to NCRA seems positive. The DOC has reported that notifications of new R&D consortia have been taking place at the rate of two or three per month. OTA was informed of only one proposed consortium in biotechnology (18). Consortial activity in biotechnology may be limited for the following reasons.

- Biotechnology is in an early and highly competitive stage, in which patentable processes and know-how are of great importance,
- R&D Limited Partnerships have offered biotechnology firms substantial resources as an alternative to R&D consortia.
- Biotechnology is characterized by rapid technological change, high growth, and private companies with intensive internal R&D activities. The need for widespread collective activities may just be emerging (14).

TAXES AND INVESTMENT

High-technology industries, such as biotechnology, are often characterized by higher levels of R&D investment than other industries. Tax relief is one of the methods the Federal Government uses to reduce the financial burden on R&D-intensive industries. This is based on the premise that such investment results in public benefits and in a greater rate of industrial innovation than would have occurred otherwise (l). Biotechnology industries rely on tax incentives because of the high levels of R&D necessary to develop and commercialize products. At present, it is difficult to assess the extent to which commercialization and development decisions in the biotechnology industries have been affected by the Tax Reform Act of 1986 (TRA) (Public Law 99-514). The difficulty is due, in part, to the small number of biotechnology companies that are realizing a profit. As more products reach the marketplace, tax planning will become a higher priority for them (6). Some analysts maintain that the revised tax incentives have only affected the distribution of investment, not the total amount of money available for investment (21). For example, RDLPs were originally predicted to disappear because the TRA virtually abolished tax shelters. Yet interest in RDLPs has prevailed. Perhaps this is because they no longer advertise themselves as tax shelters, rather they now emphasize their ability to produce income for the limited partner.

Theories on the effect of the TRA on business investment are abundant. Many in the business community believe that their tax burden has been increased to offset lowered individual tax rates. The TRA altered several of the investment incentives that were adopted under the Economic Recovery Act of 1981 (ERTA) (Public Law 97-34). An aim of TRA was to “level the playing field” for investment, thus creating a more efficient and equitable system (29). Several tax analysts have concluded that high-technology industries were not affected as much as some other industrial sectors. The initial predictions of disaster for the biotechnology industries resulting from TRA have abated.

Capital Gains

One of the most significant impacts of the TRA on the biotechnology industries is its effect on the preferential treatment of capital gains. Prior to the TRA of 1986, gains from selling stocks were preferred over the actual stock dividends. If an asset had been held for 6 months or longer, 60 percent of the gain was not taxed (30). Long-term gains were those held for more than 6 months. Under TRA, the distinction between long- and short-term tax gains was abolished at the end of 1987. Gains and income are now taxed at the same rate.

This is important to investment in the biotechnology industries because the tax treatment of capital gains was a primary attraction for investors in both RDLPs and venture capital companies. Because the returns from venture capital are mostly in the form of capital gains, some see the venture capital method of funding becoming unpopular to investors. For example, under the old treatment of capital gains, 60 percent of long-term gains from the sale of capital assets were not taxed. The remaining 40 percent were taxed at ordinary rates, which did not exceed 50 percent. This meant that the maximum tax on capital gains was 20 percent, compared to the 50 percent maximum rate on ordinary income (4).

Stock Incentive Option

Prior to TRA, it was common for biotechnology companies to offer their employees incentive stock options. **This was beneficial to the employee because the gains on stock options were treated as capital gains rather than ordinary income. Because TRA now taxes any gains received from the sale of stocks as ordinary income, the benefits and the attractive ness of incentive stock options have been reduced.**

In a 1987 workshop held by the Industrial Biotechnology Association, biotechnology industrialists were given ideas on how to restructure their employee incentive programs. Incentive programs have been important for attracting top employees to small biotechnology companies. Since smaller companies cannot compete with the large corporations in salaries, they had offered considerable incentive option packages. It is now recommended that biotechnology companies offer either cash compensation or non-qualified stock

Public Law 99-514
99th Congress

An Act

Oct. 22, 1986
[H.R. 3838]

To reform the internal revenue laws of the United States.

Be it enacted by the Senate and House of Representatives of the United States of America *in Congress assembled,*

Tax Reform Act of 1986.
26 USC 1 et seq.

SECTION 1. SHORT TITLE; TABLE OF CONTENTS.

(a) SHORT TITLE.--This Act maybe cited as the "Tax Reform Act of 1986".

(b) TABLE OF CONTENTS.—

options. These options can be deducted by the company when sold (6).

R&D Tax Credit

The original R&D credit was first adopted under ERTA at a 25 percent incremental rate. It expired at the end of 1985, and was extended for 3 years under TRA at the lower level of 20 percent. In response to criticisms that the definition of "qualified research" had caused companies to reclassify some expenditures as R&D, Congress narrowed the definition to exclude non-research activities. Under TRA, "qualified research" must be "technological in nature" (not social science) and its applications must be useful to the taxpayer in the development of a new or improved business component (20). The R&D credit's definition now places greater emphasis on innovation in research.

The provisions provide a 20 percent credit in excess of the average amount of R&D expenditures for the previous 3 years. The incremental nature of the credit ties it to increasing research expenditures rather than total expenditures made in a year, thus encouraging companies to increase their R&D commitment. Qualifying expenditures include in-house expenditures for R&D wages and supplies and 65 percent of the amount paid for contract research. Equipment expenditures do not qualify. **The R&D tax credit has been of little use to many biotechnology companies because they are not profitable enough to generate a credit.**

The credit will expire again at the end of 1988, and Congress will have to decide whether to continue extending it or to make it a permanent part of the US. Tax Code. Those in favor of the credit's permanency are also requesting a restored rate of 25 percent, arguing that the temporary status of the credit reduces its reliability to R&D planners.

Basic Research Tax Credit

The basic research credit was adopted under TRA to encourage and increase spending on basic research at universities and other nonprofit scientific and grant research institutions by businesses. The credit allows companies to deduct 20 percent for research grants, contributions, and contracts under written agreement at universities or nonprofit institutions. Equipment and services for basic research are not included under this credit; only cash funding will be eligible (20). This credit differs from the R&D tax credit in that it is not tied to increased spending levels, but can be applied to the total sum of contract payments. Provided that the payments exceed the fixed minimum base level, a company engaged in multiyear research contracts can take the credit each year (10). The fixed minimum base level is referred to as the "qualified organization base period amount" and is comprised of a maintenance of effort amount plus one percent of the company's average annual research.

Basic research that is eligible for this credit is not eligible for the R&D tax credit. However, basic research that is not claimed under the credit because it does not exceed the qualified organization base period amount, can be taken under the R&D credit as contract expenses. This credit will expire along with the R&D tax credit at the end of 1988, at which time a decision will be made on its impermanent status. While opponents argue that these credits add to the federal budget deficit through revenue loss, proponents cite the benefits to the economy of enhanced cooperation between private industry and universities.

Investment Tax Credit

First instituted in 1962, the investment tax credit (ITC) was one of the specific tax incentives that the Federal Government established to encourage investment in physical plants and equipment. It allowed a company to deduct a 10 percent credit for the cost of qualified property that was either constructed or purchased.

The repeal of the ITC will adversely affect future investment in equipment. The ITC provided a considerable financial advantage to companies and was particularly helpful for start -up companies with large equipment investments. Some financial analysts believe that reduced tax rates for corporations were supposed to compensate for the repeal of the ITC. Lowering the tax rate benefits those companies large enough to qualify, but does little to help small biotechnology companies

with little or no profit. Effective tax rates in areas related to technological innovation and R&D investment will be increased by these provisions (36). and may negatively affect the biotechnology industries over time.

Expensing and Depreciation

Another area that was targeted by tax reformers was depreciable assets. Before TRA, deductions for depreciable assets like equipment were often taken before the assets depreciated. However, under the new tax law depreciation rates were slowed down for most assets, reducing the value of the depreciation deduction from a company's taxable income. When combined with the repealed ITC, the TRA may have actually increased the tax burden for equipment investment (6,9). One option used by small businesses is not to take the depreciation and instead take a tax deduction in that year, called expensing, for equipment purchases. In a study on the effects of TRA on technological innovation, the Congressional Research Service called the expensing of intangible costs the most important tax incentive for R&D spending **(16).** Intangible costs are things such as salaries, supplies, R&D, and marketing; tangible costs usually refer to equipment and buildings.

SUMMARY

Issues of export controls and national security continue to concern some biotechnology industrialists pursuing international markets. The Drug Export Amendments Act of **1986** is seen as a means of assisting biotechnology companies in gaining access to foreign markets. The ultimate impact of these amendments has yet to be determined. Currently, the Department of Commerce and the Department of Defense are examining the roles of the Commodity Control List and the Militarily Critical Technologies List on high-technology exports, including biotechnology products. **As biotechnology produces more products for exportation, industry is concerned that the licensure process will slow to the detriment of U.S. industry.**

Biotechnology has become an essential tool of many industries. Thus, there is no such entity as "the biotechnology industry." **Biotechnology is a tool employed by several sectors. Each sector faces its own unique advantages and hurdles in the commercialization process. As biotechnology becomes fully integrated, it is often subsumed into the financial markets, regulatory requirements, patent issues, and personnel needs faced by those industries It is evident, however, that regulatory and patent uncertainty regarding biotechnology may present a temporary slowing of commercialization as new protocols are worked out.**

At present, uncertainties about Federal regulation are being resolved and ambiguities identified. It is likely that biotechnology faces a much different and more stringent regulatory environment than other high-technology sectors. It is too early to assess the impact of regulation on commercial biotechnology, but it can be assumed that regulation will increase the cost of performing R&D and doing business generally.

Current patent battles will set many precedents for future rulings. It is likely, however, that patent litigation in biotechnology will increase given the complex web of partially overlapping patent claims, high-value products, prior publication, and simultaneous production of a product by many companies. And, as patent battles are faced domestically, biotechnology companies will increasingly confront dilemmas of international patent protection. Finally, although trade secrecy is being sought by many companies in addition to patent protection, it is not the desirable route and is considered an unfortunate alternative by many biotechnology patent attorneys.

OTA did not find evidence that the threat of antitrust violations has impeded collaborative efforts in the private sector. One group of industrialists has initiated discussions about the future of private R&D consortia in biotechnology.

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