Biotechnology in Pharmaceuticals: The Japanese Challenge

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Summary. The products of biotechnology are being developed for new diagnostics and therapeutics, and it is predicted that they will have great impact on the pharmaceutical industry. In the United States, pharmaceutical companies are incorporating biotechnology into their research and development programs, often with the contractual assistance of small biotechnology firms. Their strongest competition is arising in Japan, where there are now concerted government and industry efforts to expand biotechnology capabilities and to optimize commercialization. Strategies used by the United States and Japan to incorporate biotechnology into their pharmaceutical industries are examined and compared.

The pharmaceutical industry in the United States has enjoyed steady growth and stability throughout most of this century. In 1984 the industry posted greater profit margins than any other industry group (*1*). However, the industry is also undergoing great change, largely because of biotechnology. The use of living cells to produce commercial products is having a major impact on the drug industry, with the anticipation of there being new products, new processes, new entrants into the industry, and increased competition.

Pharmaceutical companies are now taking action to address the impact of biotechnology. How they incorporate the new technologies and how they face new competition may play a significant role in defining their financial success in the future. Of the new forms of competition confronting U.S. firms, the strongest is projected to be from Japan (*2, 3*). Current strategies used by U.S. and Japanese firms to incorporate biotechnology are the focus of this article.

Impacts of Biotechnology

Traditionally, pharmaceuticals have been manufactured through chemical synthesis or purification processes. Genetic engineering makes it possible to manufacture a host of new molecules with projected uses as therapeutic agents. Among those currently under development are the interferons, interleukins and other lymphokines, tissue and kidney plasminogen activators, and tumor necrosis factor. Other biotechnologically produced therapeutics, previously made by other methods, include human insulin, growth hormone, serum albumin, and clotting factor VIII. These proteins can be produced in abundance by genetic engineering techniques and may have fewer side effects than do proteins derived from nonhuman sources (*4, 5*). Moreover, new processes can be employed to produce vitamins, amino acids, steroids, antibiotics, enzymes, bioactive peptides, and many other molecules for potential use as drugs, as well as novel compounds for use as vaccines (*6, 7*). Products of hybridomas, such as the monoclonal antibodies, are already important for use in new, sensitive diagnostics. In addition, monoclonal antibodies with therapeutic uses are on the horizon. At present, insulin is the only therapeutic entity developed by biotechnology approved for human use in the United States. In comparison, approximately 100 monoclonal antibodies have been approved for use in diagnostics. Many additional compounds are in various stages of development or testing, and they should reach the marketplace within the next decade (*2, 6*).

Another impact of biotechnology will be in pharmaceutical manufacturing. In many instances, it should be possible to produce molecules with higher purity, and perhaps more cheaply, through cell growth and fermentation processes (*2, 5–8*). This will not be without cost; new production facilities must be built at an expense of up to $100 million each (*6*), and bioprocess engineering personnel must be trained or hired.

Most U.S. and foreign pharmaceutical companies are aware of the scientific and financial importance of biotechnology, and they are in the process of incorporating biotechnology skills into their programs and plans. In 1983 the worldwide market for pharmaceuticals was over $60 billion (*9*), and biotechnology may eventually affect the production of 20 percent of the current pharmaceutical products (*6*). In addition, sales of new drugs and diagnostics made possible by biotechnology are predicted to reach $10 billion within the next decade, and they should rise thereafter (*2*). With such large markets at stake, pharmaceutical companies in the United States are attempting to be strong competitors in biotechnology. But can these companies continue to enjoy profits and growth with new competition on the horizon?

Biotechnology Industry

Fermentation processes have long been in commercial use. In the early 1970's genetic engineering and hybridoma technologies were developed, primarily in academic laboratories (*2, 5*). Subsequently, many small biotechnology firms were formed, often by academic scientists, to commercialize advances made in basic research (*2, 5*). A 1984 compilation in *Genetic Engineering News* listed over 300 companies with major biotechnology efforts, the vast majority of the companies being small and recently formed (*10*). More than half of these new companies are involved in pharmaceutical or diagnostic development (*2, 10*). More than 75 percent of these biotechnology firms worldwide have been formed in the United States, with an initial total investment of $2 billion to $2.5 billion (*3, 7, 10*). To provide a return on this investment, the new companies have entered into contract research, as well as the licensing of products they develop. Some are also attempting to directly market their products, but most do not have available the extensive resources necessary to take a pharmaceutical product through the regulatory process; nor do they have the necessary production or marketing expertise (*2, 11*). Thus, much of the effort of these small firms can be described as technology transfer to larger companies.

An analysis of strategies used by pharmaceutical companies to incorporate

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biotechnology yields three categories: (i) academic relationships, (ii) internal expansion, and (iii) agreements with biotechnology firms (*12*). All three strategies are used by many companies but the most frequently used one is the third—agreements with biotechnology firms (*2, 12*). Joint projects between large U.S. pharmaceutical companies and biotechnology firms (Table 1) should lead to the commercialization of a number of important products of biotechnology within the next decade (*2, 12*).

New Competition

The U.S. pharmaceutical industry is comprised mostly of large, established companies that have been responsible for the development and introduction of many major drugs. As a result of biotechnology, there should be major changes in the composition of the industry in the form of new competition.

One major source of competition will be large, nonpharmaceutical firms that have planned a future in pharmaceuticals through biotechnology programs. Companies such as Monsanto and Du Pont, which currently have only modest sales related to pharmaceuticals, have announced major expansion of their drug and diagnostic research efforts with emphasis on biotechnology. Table 2 demonstrates that, in addition to drug companies, there are large, nonpharmaceutical companies that are also buying equity positions in biotechnology firms. The new technologies also are important for future products in the chemical industry; nine of the ten largest U.S. chemical companies have annonced their involvement in biotechnology for the development of agrichemicals and pharmaceuticals (*13*). Large companies with current emphasis on chemicals, foods, textiles, and other goods could become prominent contenders in the pharmaceutical industry of the future.

A second source of competition will be from the biotechnology firms themselves. Although most do not have the capital to bring a drug to market, many of these firms do have the ability to market diagnostics. Through financial incentives, such as research and development limited partnerships (RDLP's), biotechnology firms may obtain the capital to directly market therapeutics in the future (*2, 14*). In each year from 1982 to 1984, a total of $166 million to $199 million was raised by five to nine firms to form RDLP's that involve the development of specific biotechnology-based products (*14*).

Foreign Competition

The strongest source of competition in biotechnology for U.S. companies appears likely to come from abroad. Whereas the United States has no significant federal program for the coordination of biotechnology efforts, the governments of Great Britain, France, West Germany, and Japan have mounted major programs for the growth of domestic biotechnology (*2*). The country predicted to have the greatest potential impact on the commercialization of biotechnology is Japan (*2, 3*). Although the new biotechnologies have been largely developed in the United States, the Japanese are expected to soon take the lead in commercialization of these technologies (*2, 3*). A large part of their success will be based on products first developed in the United States. An analysis of Japan's incorporation of biotechnology may help in understanding this process.

Strategies Used by the Japanese

Historically, the Japanese pharmaceutical industry has been quite different than that in the United States, as is indicated in Table 3. Japanese drug companies are considerably smaller than their U.S. counterparts; there are 11 U.S. drug companies with annual pharmaceutical sales (1983) of over $1 billion, but only one Japanese company, Takeda, has reached that mark (*15*). In the past, U.S. companies were responsible for the introduction of twice as many new drugs as Japanese firms (*2, 9*). In recent years, however, Japanese pharmaceutical companies have spent almost 50 percent more on research and development (as a proportion of sales) than U.S. companies (*1, 9*). As a result, Japanese companies introduced 70 percent more new drugs between 1981 and 1983 than did U.S. companies (*2*). Given the total amount spent on research and development, the Japanese have been at least six times more productive (as measured by number of drugs introduced) per dollar spent on research (*16*). A recent estimate from the Japanese Bio-Industry Development Center predicts $60.7 billion in biotechnology-related Japanese sales by the year 2000, with $12.8 billion coming from pharmaceuticals (*17*), confirming Japan's emphasis on biotechnology.

Japan is considered a world leader in fermentation technology (*3, 5, 17*). This is of key importance to commercial success in biotechnology, but basic research is also necessary to supply new products for companies to market. Recent Japanese progress in biotechnology has resulted from coordinated efforts by the government, individual companies, and academic laboratories. Moreover, Japanese companies have received considerable foreign help, mostly from the United States, in filling certain gaps in basic research and development.

Japanese government programs in biotechnology have emerged from three sources: the Science and Technology Agency (STA), the Ministry of International Trade and Industry (MITI), and

Table 1. Joint projects between large U.S. pharmaceutical companies and biotechnology firms. Interactions announced between 1981 and 1984, selected from database (*12*). Two Swiss-based companies, Hoffmann–La Roche and Sandoz, that have major facilities in the United States are also included.

Biotechnology firm	Pharmaceutical company	Products involved
Biogen	Merck	Hepatitis B vaccine
	Schering-Plough	Interferon
	SmithKline	Anticlotting factor
Centocor	Abbott	Cancer diagnostics
	Hoffmann–La Roche	Monoclonal antibodies for cancer treatment
	Warner-Lambert	Hepatitis B diagnostics
Collaborative Research	Sandoz	Kidney plasminogen activator
Genentech	Hoffmann–La Roche	Interferons
	Lilly	Insulin
	Baxter Travenol	Diagnostics
Genetic Systems	Syntex	Diagnostics
Genetics Institute	Baxter Travenol	Factor VIII
Genex	Bristol-Myers	Interferons
Hybritech	Baxter Travenol	Monoclonal antibodies for bacterial infection
Molecular Genetics	Lederle	Herpes simplex vaccine

Table 2. Equity purchased in firms with a major focus on biotechnology. Equity purchases selected from database (*12*).

Large company (purchaser)	Biotechnology firm	Year
	Purchased by U.S. pharmaceutical companies	
Abbott	Amgen	1980
Baxter Travenol	Genetics Institute	1982
Becton Dickenson	Applied Biosystems	1984
Johnson & Johnson	Enzo Biochem	1982
Lederle	Molecular Genetics	1981
Lederle	Cytogen	1983
Lilly	Synergen	1984
Schering-Plough	Biogen	1982
Schering-Plough	DNAX Ltd.*	1982
SmithKline	Beckman*	1982
Syntex	Genetic Systems	1982
	Purchased by other U.S. companies	
Dow	Collaborative Research	1981
Du Pont	New England Nuclear*	1981
Fluor	Genentech	1981
W. R. Grace	Amicon*	1983
Martin Marietta	Molecular Genetics	1982
Monsanto	Biogen	1980
Monsanto	Collagen Corporation	1980
	Purchased by Japanese companies	
Green Cross	Collaborative Research	1981
Mitsubishi	BioVec	1984

*Acquisition. Each nonacquisition purchase involved an average of $8 million.

Table 3. Comparison of U.S. and Japanese pharmaceutical industries and involvement in biotechnology. All 1983 data, except as noted. [Sources: (*1, 2, 9, 15*)]

Data category	United States	Japan
Population (millions)	234.5	119.2
Gross national product	$3.3 trillion	$1.2 trillion
Domestic pharmaceutical market (world rank)	$21.3 billion (1)	$13.4 billion (2)
Number of pharmaceutical companies with sales over $1 billion*	11	1
Total pharmaceutical sales of ten largest pharmaceutical companies†	$16.7 billion	$6 billion
Pharmaceutical sales as percent of total sales‡	50.1	74.1
Number of new pharmaceutical products introduced:		
1961–1980	353	155
1981–1983	24	41
R&D expenditures as percent of sales‡	6.8	9.2
Scientists and engineers in industrial R&D§:		
Total number	573,900	272,000
Percent of work force	0.58	0.50
Government-funded research in biotechnology:		
Total	$520 million	$60 million
Percent of basic research	>98	<50
Targets of funding in biotechnology	Basic research	Basic research, scale-up, industrial projects, government laboratory facilities, manufacturing technology

*Pharmaceutical sales only. †Total world pharmaceutical sales in 1983 were approximately $60 billion. ‡Average of top ten companies. §All industries, 1977 data.

the Ministry of Agriculture, Forestry and Fisheries (MAFF) (*2, 18*). The total government support for biotechnology, $50 million to $60 million in 1984, is only about one-tenth of that spent by the U.S. government (Table 3) (*2, 18*), but Japanese funding is much more focused on specific projects. For example, MITI, in a 10-year strategic program beginning in 1981, has targeted next-generation technologies to foster scale-up techniques, aimed at assisting in the commercialization of biotechnology (*2*). The STA is also funding applied research, such as the development of bioreactors (*2*). The latest announced budgets of STA, MAFF, and MITI are emphasizing national centers related to biotechnology research, including the development of cell line and gene banks (*18*). Very little of the Japanese government's support for biotechnology is for basic research (*2*). In contrast, the U.S. government's support of biotechnology is almost ten times more, but support of applied research makes up only 1 to 2 percent of this total, with far less specificity than in Japan (Table 3) (*2*).

Another emphasis in Japan is to foster cooperation between companies and between industry and academia. There are more than a dozen joint ventures on record involving two or more Japanese companies that are aimed at developing therapeutics through research in biotechnology (*2, 19*). Similar cooperation between large U.S. companies does not (or cannot) exist (*2*).

In order to further foster cooperation between Japanese companies, a trade association, tentatively called the Society for Advanced Pharmaceutical Research, was formed in 1985 with 31 member companies and the support of Japan's Ministry of Health and Welfare (*19*). A trade group, the Industrial Biotechnology Association, exists in the United States with 46 member companies, but is not supported by the federal government (*20*).

Because government funding in Japan is focused on applied research, Japanese companies are also in the process of expanding in-house expertise in basic research and development in biotechnology. Many companies have announced the expansion of research facilities, such as Sankyo's new $53-million biotechnology laboratory to be completed by 1986 (*21*). The availability of personnel to staff basic research laboratories in Japan has been a problem, primarily owing to a paucity of university programs in molecular genetics (*2, 16*). To fill the need for researchers, some Japanese companies

have begun in-house training programs, while others have sent employees abroad to be trained or have hired foreign researchers (*2*).

These methods are apparently successful; the number of in-house scientists involved in basic research in biotechnology has increased more than fivefold in the past 3 years (*16*). Japan has an ample supply of fermentation process engineers, which is important for the commercialization of biotechnology (*2, 16, 22*). In contrast, in the United States the supply of basic researchers for biotechnology has not been as much of a problem, although it is expected that there will be a shortage of scientists trained in bioprocess engineering (*2, 16, 22*).

In Japan, little venture capital has been available and very few biotechnology firms have been formed (*2, 16, 23*). With in-house incorporation of biotechnology still at an early stage, Japanese companies have turned to U.S. biotechnology firms for basic research assistance. Table 4 identifies a number of these contractual agreements, some of which involve the same U.S. biotechnology firms and the same products as covered by agreements with U.S. pharmaceutical companies (see also Table 1). In most cases the contractual agreement gives the Japanese company licensing rights to a product developed in the United States, often with marketing rights being limited to Japan and other Asian countries (*2, 16, 24*). In only a few instances have Japanese companies purchased equity in biotechnology firms in the United States (Table 2).

To assess the extent of both domestic and foreign involvement with U.S. biotechnology firms, I have created a database of recorded pharmaceutical-related interactions between these firms and large companies (*12*). This database includes 72 joint or contractual interactions between U.S. biotechnology firms and U.S. companies from 1981 to 1985. Additionally, the database includes 43 such interactions between U.S. biotechnology firms and Japanese companies, 60 percent as numerous as those with U.S. companies (*12*). It is clear that Japanese companies, like large U.S. companies, are relying on contractual agreements with small U.S. firms to provide basic research or newly developed products (*2, 16, 25*).

Some U.S. biotechnology firms have set up facilities in Japan to coordinate joint research with Japanese companies. For example, Genentech Ltd. was set up in Japan in 1982 to serve as a liaison between Genentech in the United States and multiple Japanese firms with which it does business (*26*).

As has occurred in the United States, Japanese companies not previously involved in pharmaceuticals have started biotechnology programs that could lead to pharmaceutical products. A recent listing noted 10 major Japanese chemical companies, 15 food processing companies, and 4 textile companies that have biotechnology-related pharmaceutical projects (*2*). Most of these companies have contractual agreements with U.S. biotechnology firms (*12*).

In increasing numbers, large U.S. companies are forming joint subsidiaries with Japanese companies for the commercialization of pharmaceuticals, as evidenced by such company names as Merck-Banyu, Pfizer Taito, Nippon Upjohn and Du Pont–Sankyo (*15, 27*). Other joint agreements, not involving the formation of subsidiaries, have been recorded with U.S. pharmaceutical companies, such as Shionogi's agreements with Lilly and Merck (*12, 24*). In addition to U.S. companies entering Japan, at least one Japanese pharmaceutical company is setting up a biotechnology facility in the United States. Otsuka, Japan's fourth largest pharmaceutical manufacturer, is building a $7-million biotechnology research facility in Maryland, to be completed in 1985 (*28*). Other Japanese pharmaceutical companies already have or plan manufacturing facilities in the United States; they include Takeda, Japan's largest pharmaceutical company, which has a plan for a vitamin-production facility in North Carolina.

United States and Japan: Comparison of Strategies

In comparing the incorporation of biotechnology into the U.S. and Japanese pharmaceutical industries, some similarities are apparent. Companies in both countries have expanding in-house biotechnology efforts, but are also relying on the new biotechnology firms, primarily U.S. ones, to gain access to basic research in biotechnology and to obtain products for commercialization. This method appears successful; many initial products of these collaborations are in the pipeline for approval by the Food and Drug Administration (*29*). For example, human insulin, the first therapeutic developed by biotechnology, was evolved by Lilly in collaboration with Genentech; and alpha interferon, to be marketed by Schering-Plough, was developed by Biogen (*4, 6*).

In both countries there is new pharmaceutical industry competition attributable to biotechnology. Nonpharmaceutical companies, such as Exxon, Corning, W. R. Grace, Monsanto, Martin Marietta, and Du Pont, have planned major programs in biotechnology (*2, 12*). Giant Japanese corporations, such as Mitsubishi Chemical, Ajinomoto, Suntory, Kirin Brewery, and Asahi Chemical Industry also are in the process of developing pharmaceutical products employing biotechnology (*2, 12*). It is thus likely that the composition of the pharmaceutical industry in both countries will change radically over the next decade.

Where Japan and the United States

Table 4. Contractual agreements between U.S. biotechnology firms and major Japanese companies. Agreements announced between 1981 and 1984, selected from database (*12*). Abbreviations: HSA, human serum albumin; IL-2, interleukin-2; MAb, monoclonal antibodies.

Biotechnology firm	Japanese company	Products involved
Biogen	Shionogi	Interferon, IL-2, HSA
	Fujisawa	Tissue plasminogen activator
	Green Cross	Hepatitis B vaccine
	Suntory	Tumor necrosis factor
	Teijin	Factor VIII
Centocor	Toray	Hepatitis diagnostics
Collaborative Research	Green Cross	Urokinase, interferon
Genentech	Mitsubishi	Tissue plasminogen activator
	Toray	Interferons
Genetic Systems	Daiichi	Diagnostics for blood disorders
Genetics Institute	Chugi	Human erythropoietin
Genex	Yamanouchi	Fibrinolytic agent
	Green Cross	HSA
	Yoshitomi	IL-2
	Mitsui Toatsu	Urokinase
	Mitsubishi Chem.	HSA
Hybritech	Teijin	MAb's for cancer treatment
	Green Cross	Immunoglobulins
	Toyo Soda	MAb diagnostics

differ is in the type and amount of government support for the development of biotechnology. In Japan there is a clear effort by government to enhance the future commercial success of the pharmaceutical industry by assisting in the development of biotechnology. Although this support is administered by a few different agencies and is small in size (by U.S. standards), it is viewed both externally (*2, 25*) and internally (*16*) as a single cohesive effort with a high potential for success. The companies involved must create their own basic research and development programs; government assistance is at the next level, helping to foster commercialization of products, manufacturing, and generic support, such as gene banks (*18*). In the United States, federal support for biotechnology is ten times greater in magnitude and is aimed at basic research. Although support of basic research programs in biotechnology should be continued and expanded to ensure maintained leadership in basic research, support for more applied areas is also needed (*2, 16*).

Another contrast between the two countries is in the availability of basic researchers in biotechnology and bioprocess engineering. There was a reported shortage in the United States of basic researchers trained in genetic engineering, but this problem appears to have abated (*2, 30*). Due to strong academic programs in this and related areas, the availability of basic researchers should continue to be sufficient (*2*). However, a paucity of academic programs in bioprocess engineering continues (*2*). As more companies generate products of biotechnology for scale-up, it is expected that there will be a severe shortage of personnel trained in production technologies, which may hamper commercial success (*2*). Japan has the opposite problem—an adequate supply of fermentation engineers but too few basic researchers with training in molecular genetics (*16*). This is another reason why Japanese companies have been borrowing U.S. basic research, but are predicted to outpace the United States in commercialization (*2, 3*).

Outlook

In January 1984 the U.S. Congress Office of Technology Assessment (OTA) published a 612-page analysis on commercial biotechnology (*2*). The report noted the importance of biotechnology both for its basic scientific benefit and for its potential commercial development. In assessing the competitive position for the United States, the OTA report stated the following (*2*, p. 7):

> Japan is likely to be the leading competitor of the United States for two reasons. First, Japanese companies in a broad range of industrial sectors have extensive experience in bioprocess technology. Japan does not have superior bioprocess technology, but it does have relatively more industrial experience using old biotechnology, more established bioprocessing plants, and more bioprocess engineers than the United States. Second, the Japanese Government has targeted biotechnology as a key technology of the future, is funding its commercial development, and is coordinating interactions among representatives from industry, universities, and government.

When the focus of analysis is narrowed to the pharmaceutical industry, it can also be concluded that the Japanese have the potential to be a leading competitor. An important factor in their success has been the borrowing of basic biotechnological research by Japanese companies from U.S. biotechnology firms. Although biotechnology licensed by U.S. firms to Japanese companies generally involves marketing rights in Japan or Asia (*2*), the Japanese market for pharmaceuticals is the second largest in the world. When added to other Asian markets, it becomes two-thirds the size of the North American or European markets (*9*). U.S. pharmaceutical companies have gained 40 percent of their revenues from foreign sales, and the loss of a foreign market may represent lost income (*9*).

In addition to basic biotechnology borrowed from the United States, Japan has been simultaneously building its own strength in this field. There are more and more frequent reports of new developments in basic biotechnology and discoveries of new drugs from Japanese industrial laboratories (Table 3) (*12*). It is thus possible that Japan's predicted future strength in pharmaceutical biotechnology will come both from internal developments and strategic government programs (*16*).

This is not to imply that with Japanese strength in biotechnology will come U.S. weakness in this area. As stated earlier, pharmaceutical and other companies in the United States are expanding their efforts in biotechnology and are nearing their goals of bringing new therapeutics and diagnostics to market. However, an analysis of Japanese strategies may help to understand how U.S. industry can optimize this process. In addition, U.S. industry will be strengthened if the U.S. government makes the commercialization of biotechnology a high priority and funds specific academic and other programs leading to that goal (*2*). As stated in the OTA report (*2*): "The United States may compete very favorably with Japan if it can direct more attention to research problems associated with the scaling-up of bioprocesses for production."

In addition, government activities that enhance cooperation between companies, decrease regulation, or provide centers to assist in biotechnology would help meet this goal (*2, 6, 31*). However, in the period since the OTA report was made public, no broad program of support to strengthen the U.S. position in biotechnology has been announced by the federal government.

Steps in the Right Direction

A few recent developments should prove useful to the future development of biotechnology in the United States. The first is the opening of biotechnology centers to assist in the transfer of biotechnology expertise from academia to industry. Two of these centers are at Pennsylvania State University and in Research Triangle Park, North Carolina. The Penn State Biotechnology Institute has planned research and educational facilities and will allow member companies access to "application-oriented research" and to a pilot production facility for assistance in scale-up (*32*).

The North Carolina Biotechnology Center currently receives $2.5 million in annual funding from state, federal, and industrial sources. The center funds specific programs, such as its Monoclonal Lymphocyte Technology Center, which involves academic research at the University of North Carolina and Duke University, the participation of industry, and funding by the National Science Foundation. The five industrial members agree on priorities for directed research to be funded by specific grants to participating laboratories. Although still in its infancy, the Monoclonal Lymphocyte Technology Center is fostering cooperation between companies in a university environment that probably would not have otherwise occurred (*33*).

The Center for Advanced Research in Biotechnology (CARB), to be built in Gaithersburg, Maryland, will combine federal, state, county, and university efforts (*34*). With CARB, the National Bureau of Standards will add its analytical expertise to molecular biology expertise from the University of Maryland. A CARB research facility to be completed

in 1986 will house 130 scientists. In addition to basic and applied research in biotechnology, CARB will provide services to industry, including analytical measurements and molecular modeling on a supercomputer, and it will make available basic tools for research in biotechnology (*34*).

Lastly, the National Science Foundation has announced a $20-million, 5-year grant to establish the Center on Biotechnology Process Engineering at the Massachusetts Institute of Technology (*35*). This is part of a new program to advance engineering research with industrial applications. It is likely that industry will also provide support for this center (*35*). Although not part of a broad program to develop biotechnology, the creation of this center, CARB, and other biotechnology centers will greatly assist U.S. companies in developing the skills necessary to face competition.

Conclusions

The current situation involving biotechnology in the U.S. pharmaceutical industry and its competition can be summarized as follows: Many if not most of the significant advances in biotechnology over the past decade have occurred in academic laboratories in the United States. A large portion of this research has been funded by the U.S. government, currently at an annual rate of more than $500 million. As the commercial potential of the products of biotechnology has become apparent, these products and many of the researchers have been transferred to a new industry—the biotechnology industry. This fledgling industry has been formed with over $2 billion of venture capital, mostly from the United States.

A problem occurs with return on investment. The new biotechnology firms need income to remain in business, and, for the most part, they are not presently able to market their products directly. However, they can sell their research capabilities and rights to products.

The U.S. pharmaceutical industry will benefit greatly from these discoveries, but it does not have exclusive access. On the one hand, many other U.S. companies see this as an opportunity for future profits and a means to enter the pharmaceutical industry. On the other hand, many Japanese companies, poised with enormous fermentation expertise to commercialize the products of biotechnology, see this as an opportunity to buy products of basic research while developing basic research capabilities of their own. The investment to develop biotechnology has been made primarily in the United States, yet the commercial success of this research will be shared with companies from other countries, especially Japan. The dollars invested by the United States should lead to U.S. jobs and increased revenue for U.S. corporations, but some of that return will be lost. And Japan, with U.S. help, is predicted to soon become the leading competitor in this field.

It is not a question of whether biotechnology research should be supported; the benefits to mankind are large. However, the type of support can clearly affect the outcome. In addition to the continued support of basic research, a U.S. federal program needs to be strategically designed to foster academic, government, and industry programs that would lead to maximizing the commercial success of biotechnology within the United States. If this occurs, then the predicted future leader in both scientific advances and commercialization could be the United States. Without relation to defense, it is unlikely that the transfer of basic biotechnology will be highly regulated or curtailed in the future. However, it should be possible to borrow strategies from Japan for planning and coordinating the commercial success of technologies, present and future.

Biotechnology in the pharmaceutical industry is still at a very early stage. It may still be possible for U.S. industry to maximize the return on investment in basic research. New programs that emphasize shared knowledge and centralized facilities should assist industry in its ability to develop new therapeutics. Of key importance is the assistance provided by the federal government to optimize regulatory and financial environments and to furnish coordinated support for continued achievement in biotechnology research.

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