Chapter 10

Science and Technology Policies

"It is my personal conclusion that no plans, either present or contemplated, will prevent our gradual loss of leadership in biotechnology unless they provide for extensive and fundamental changes in the conduct of government supported research in the United States."

Norman G. Anderson
hearing before the Technology Policy Task Force, July 1987.

"A rosy glow has long suffused our vision of biotechnology in Japan: government support, public acceptance, highly motivated researchers, the happy reports of American research executives with joint development agreements—it sounded ideal, a model and a challenge. So it was a shock to discover. . . that the country may not be the land of tPA milk and recombinant honey."

Douglas McCormick
Bio/Technology, July ***1989***

"Although the EC has the human, scientific and material resources to compete globally in the biotechnological race, it has failed so far to match strides with its main rivals-the United States and Japan. "

The European Study Service, 1991

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Science and Technology Policies

INTRODUCTION

For most governments, including the United States, research spending serves diverse goals. Enhancing national defense, improving public health, training new scientists, and ensuring an adequate food supply are four common examples. Publicly funded research in these areas is expected to support economic growth and the strength of domestic industry, in great part through the creation of a research and technology infrastructure. This infrastructure includes training young scientists and technicians through support of basic research. Some governments put less emphasis on goal-or mission-oriented research and more on encouraging a broad capacity for industry to adjust to technological change through education, development of technical standards, and decentralized research activities (10). Governments generally fund basic research, for which there is little incentive for funding in the private sector or that is beyond the financial capacity of industry. The results of such research are generally published openly and made available to everyone, regardless of nationality. Sometimes, however, governments fund research closer to the market, occasionally with the express purpose of aiding or encouraging investment by domestic industries in specific technologies.

National policies that bear on biotechnology research and training vary around the world in design and execution, for a variety of reasons. These include the state of the existing science base, structure and orientation of industry, mix of resources and markets, role of public perceptions, regulations, and relationships among government, industry, and universities.

Many countries without a previous strong foundation in the biological and biochemical sciences, for example, are building research infrastructures. Industrializing Pacific Rim countries are encouraging research and commercial activities appropriate to local and regional markets, such as hepatitis vaccine development and production. Countries without a strong tradition of university-industry cooperation have established programs to reorient the research community and encourage university-industry ties. Australia, lacking a large domestic market, encourages its firms to establish commercial ties and develop markets abroad. Denmark, with a small domestic market and research base, actively promotes international research efforts through a number of successful, international companies. Cooperative research programs between and among European countries are growing in size and, perhaps, in importance; however, their significance lies less in immediate results than in the breakdown of social, cultural, and political barriers to cooperation and in the creation of translational research networks, which are distinct European concerns.

A challenge to the adoption of a national biotechnology policy is the internationalization of research, development, and product commercialization. If basic research, by its nature, flows easily across borders, to what extent does the funding country benefit from its investment? In the emerging global research and commercial environment, aggressive companies, whether large multinationals or savvy newcomers, seek the best ideas regardless of nationality. Likewise, they produce goods and services to effectively compete in international markets regardless of nationality. It is no longer always clear what constitutes an American firm in a global economy. Because technology, goods, and capital, flow more easily across borders than people; national interest may be best defined by focusing on the education and training of the workforce, rather than on firms themselves (35).

In 1984, the Office of Technology Assessment (OTA) found that government targeting of biotechnology for special support was one of the least significant factors affecting competitiveness in biotechnology (44). This finding remains valid today. Government targeting efforts everywhere, including Japan, seem to have had marginal impact, at best. One reason may be that "biotechnology” is a buzzword whose usefulness has passed. A more accurate term is ‘biotechnologies,’ that is a series of research and industrial techniques. It is difficult to talk about biotechnology per se because the techniques have been integrated into distinct and very different industrial sectors with unique technical issues and distinct investment and market environments (45). These developments make it difficult, and possibly futile, for any nation to craft and implement a coordinated biotechnology strategy. Continued integration will make the task more difficult. More important will be the identification of key biotechnologies that need government support and industry encouragement.

Previous OTA reports have pointed out the relative underfunding in the United States of biotechnology-related agricultural, environmental, and risk assessment research, when compared with biomedicine (45). Although it has been helpful to look at biotechnology-related expenditures in different areas of application, questions raised by such analyses relate more to the differences between various fields than to biotechnology as a distinct entity. Biotechniques are an important part, but not the only part, of research in these fields. They may be significant to a number of industrial sectors but by themselves will not revolutionize existing structures. Their industrial significance, though potentially powerful, will be evolutionary and must be viewed in the context of all factors—technical, economic, and structural—affecting such industries.

This chapter looks primarily at direct government efforts aimed at promoting biotechnology research, such as funding and training of scientists. Governments also have indirect means for encouraging or discouraging industrial research, such as regulation of research and products, trade and tax policy, and intellectual property protection. These issues are discussed elsewhere in this report (see chs. 4,11, 12,13).

Photo credit: Kevin O'Connor

The Development Center for Biotechnology (DCB) is housed in this building in Taipei. DCB was established by the Republic of China in 1984 to promote biotechnology and develop internationally competitive products.

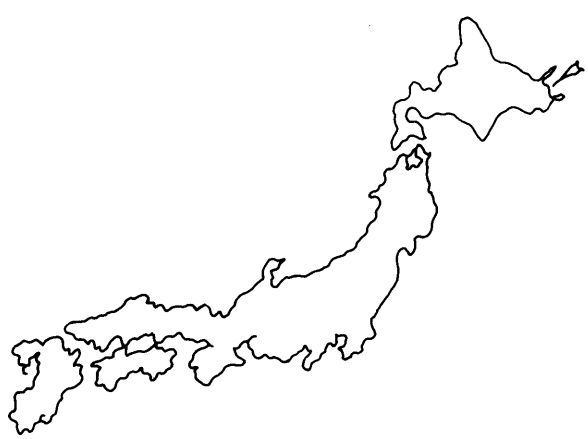
NATIONAL POLICIES

National policies to promote biotechnology research and development (R&D) can be categorized as targeted; coordinated through academia, the state, or industry; or laissez-faire. In general, countries that have targeted biotechnology for development do so because the techniques are perceived to permit economies in other industries, have important linkages to the rest of the economy, or because they might establish a niche in the international market that will yield continuing income. Although nations share a number of common issues and patterns of government involvement, specific policies, adapted to unique needs and circumstances, may not be easily adaptable elsewhere.

A number of countries, principally Japan and the Newly Industrializing Countries (NICs) of the Pacific Rim, have established comprehensive government policies strongly promoting economic growth (see box 10-A). In the United States and much of Europe, growth promotion is less prominent and is one of many competing social concerns. As a result, fundamental goals are more diffuse and, therefore, less obvious than in a country like Japan.

There is considerable disagreement over what constitutes "the Japanese model." But Japan's industrial success, the extent to which other Pacific Rim countries are trying to imitate that success, and the interest in how other countries are adopting Japanese practices, necessitate a closer look at Japanese industrial and research policies. This section, therefore, examines R&D policies in the United States, Japan, and selected European countries. Appendix A provides more detailed information of biotechnology industrial policies in several other countries.

Japan: A Targeted Approach



In 1981, Japan's Ministry of International Trade and Industry (MITI) announced that biotechnology, along with microelectronics and new materials, was a key technology for future industries. The announcement attracted interest and concern abroad, largely because of the key role MITI played in guiding Japan's economic growth in the postwar period (see box 10-B). It was frequently predicted that inclusion of biotechnology in MITI's Next Generation project, combined with a variety of incentives from MITI and other agencies (e.g., tax breaks for research investments and seed money for cooperative research projects) would prompt Japanese investment and eventual dominance in biotechnology (44).

There is little doubt that government policies, including the Next Generation project, encouraged biotechnology investment by a large variety of chemical, food, and fermentation companies, as well as by traditional pharmaceutical firms in Japan. Japanese investment in biotechnology, however, predates MITI's Next Generation project. New initiatives in the life sciences came earlier from the Science and Technology Agency (STA) and the Ministry of Education and Culture, which fund Japanese university research (7). A number of companies made substantial investments in biotechnology prior to 1981. Mitsubishi Kasei Corp. 's Institute of Life Sciences was setup in 1971, about the time that Cetus was established in the United States (49).

Regardless of earlier actions, MITI's naming biotechnology as an area of interest probably gave it the legitimacy that it previously lacked and eased financing for private investment-as it had done earlier for other industries and technologies. It seems likely that some firms entered biotechnology research as a result of government policies. It seems also plausible, however, that MITI jumped on the biotechnology bandwagon because it did not want to be left behind.

As in the United States and elsewhere, the broad range of potential biotechnology applications has led to a wide variety of, frequently overlapping, initiatives by various Japanese agencies.

Ministry of International Trade and Industry

Of 12 initial Next Generation research projects proposed in 1981, three (bioreactor, mass cell culture, and recombinant DNA application) were in biotechnology. Concomitant with these proposals was the establishment of a Biotechnology Joint Research Association consisting of 14 companies, divided into three research groups, each associated with a research institution of MITI's Agency of Industrial Science and Technology. Most of the companies were in the chemical or food business, and most of the frost product goals were recombinant DNA (rDNA) or monoclinal antibody pharmaceuticals and diagnostics (7). Takeda, Japan's largest drug firm, was the only pharmaceutical company in the Next Generation initiative and is also the only pharmaceutical company participating in the Protein Engineering Research Institute (PERI), which is discussed in greater detail below.

The MITI faced a serious organizational problem. In contrast to previous government initiatives, particularly in manufacturing technologies, the incentive for cooperation between competing firms was lessened by the problem of proprietary rights.

Box 10-A—The Asian Tigers

The Newly Industrializing Countries (NICs) of the Pacific Rim share with Japan an emphasis on export-driven growth. These countries have also developed patterns of government-industry cooperation, although these patterns differ significantly from those in Japan. There is a high degree of activism on the part of governments, particularly in Korea, Taiwan, and Singapore. All use licensing of foreign technology and repatriation of foreign-trained nationals to build their domestic research infrastructure.

Korea shares with Japan a strong bias toward applied research, apparently in large part, because of an underdeveloped research base. As in Japan, the bulk of R&D is done by industry, and several chaebols (large industrial combines) and pharmaceutical companies have facilities in the United States to transfer technology and develop their internal resources. Licensing agreements with U.S. and Japanese firms area clear part of this strategy. The government directly subsidizes some industry research, including up to 30 percent of selected proposals from member companies of the Korea Genetic Research Association (KOGERA).

In contrast, Singapore is emphasizing basic research (roughly 80 percent of that country's annual biotechnology-relevant research budget) and creation of a research infrastructure through training and repatriation. Singapore's National Program in Biotechnology also features favorable tax incentives for domestic and foreign investment. Although the program recognizes the need for multinational investment, the main goal is the development of biotechnology-based local industry. The new Institute of Molecular and Cell Biology at the National University of Singapore will have 21 research teams carrying out basic research in underlying disciplines. Glaxo, a large, British-based pharmaceutical company, will provide a $50 million trust fund to underwrite neurobiology research at the institute over the next 15 years.

Taiwan, like Singapore, is employing repatriated nationals to the fullest extent possible to help build their research base. One of the best developed research establishments in Asia is further strengthened by the large pool of Taiwanese scientists in the United States. In addition, investment capital is readily available. The country has roughly $75 billion in foreign reserve holdings, second only to Japan, and has invested in several U.S. high-technology firms. Nevertheless, Taiwan seems to be making more of an effort than Singapore to reach midstream development; roughly 80 percent of biotechnology-relevant funding is devoted to applied research. (This is probably part of a strategy to develop products, such as Hepatitis B vaccine, which are significant to domestic and regional markets.) Of all the Asian NICs, Taiwan appears to be in the best position to take commercial advantage of biotechnology. But, Taiwan's emphasis on publicly funded midstream and applied research could reflect the reluctance of Taiwanese industry, dominated by small and medium-size manufacturing firms, to invest in R&D,

SOURCE: Office of Technology Assessment, 1991, adapted from 1989 International Conference on Biotechnology in a Global Economy; and E. Richards, "Taiwan's Latest Export: Money," *The Washington Post, May 26, 1989.*

Therefore, MITI tried to focus projects on areas in which Japan seemed clearly behind the United States and Europe. The level of success achieved in these projects was disappointing. The MITI, for example, abandoned a bioreactor project, due to industry's reluctance to cooperate (49).

The years 1986 to 1988 saw the establishment of bio-industry, with MITI setting regulatory guidelines for industrial uses of biotechnology in amino acid, enzyme, detergent, and cosmetic production. Today, MITI is continuing to support R&D efforts in areas such as: marine biotechnology and biodegradable plastics, addressing relevant industrial policy (e.g., tax incentives and Japan Development Bank and Small Business Finance Corp. loans, and promotion of industry standards), improving safety measures (new contained-use regulations and developing lists of industrially exploitable organisms), internationalization (regulatory harmonization, and international R&D cooperation, and funding developing country research) (25). MITI's patent office continues to play a central role in biotechnology developments. The MITI planned to spend $58 million on biotechnology in 1990, including funding dozens of public-private research projects, ranging from waste water treatment systems to biosensors.

Ministry of Education, Science, and Culture

The Ministry of Education, Science and Culture (MESC) is the largest single source of life/science research funding in Japan. Its Bureau of Science and International Affairs administers university grants, training programs, and international exchange and collaboration. The MESC also has authority over the national universities, i.e., the Universities of Tokyo, Osaka, Kyoto, and Nogoya; the National Institute of Genetics; and the Okazaki National Research Insti-

Box 10-B—Japanese Industrial Policy

Japan's development into a major economic power was neither accidental nor inevitable. One analyst of postwar Japan argues that a system encouraging rapid economic growth resulted from three fundamental sources. First, a popular consensus on the need for economic priorities was dictated by the harsh conditions of the 1940s and Japan's unique situation: late industrialization, limited natural resources, a large population, the need to trade, and the constraints of the international balance of payments. Second, an organizational inheritance dating back to the 1930s included experiments with control of the economy, first by powerful industrial groups and then by the State. These experiences encouraged a convergence of views on the part of bureaucratic and business elites, as did cross-penetration of these elites, due to recruitment of politicians and managers from government bureaucracies. Third, a conscious pursuit of economic growth fostered the manipulation of institutions toward this end.

A system of government-industry cooperation, based on the ***zaibatsu*** working with the government over many years, became even more important following World War II. At its best, it seemed to harness intense competition between firms within agreed areas of development. Although a number of strong bureaucracies, especially the Ministry of Finance, played critical roles, it was the Ministry of International Trade and Industry (MITI) that became a kind of 'economic general staff. MITI used powerful tools, including control of foreign trade and introduction of foreign technology through the 1960s, thereby protecting domestic industry and providing domestic firms with relatively cheap, foreign technology through licensing. But, it was primarily the development of indirect market-conforming tools (particularly informal "administrative guidance' that allowed MITI to play a key role in restructuring the Japanese economy-first into heavy industries and then into knowledge-based, high-technology industries. MITI transformed itself to match Japan's changing needs and role in the global economy. It served not so much as a director of competition but, as a player itself, with its own purposes and its own means of intervening in the market to achieve its goals.

Broadly speaking, public policy in Japan has been characterized by a great degree of discretion yielded to elite and competing bureaucracies, with conflict between bureaucracies and between these bureaucracies and strong industries dominating policy development. Except for business, interest groups in the U.S. pluralistic sense have played a relatively minor role in policy development, forcing political intervention and bureaucratic change only in extreme cases. For example, in the 1960s, industrial pollution stimulated public concern and resentment.

Apart from assisting structural changes, MITI, like its prewar and wartime predecessors, and other agencies, such as the Ministry of Health and Welfare, have encouraged improved management, production techniques and applications of new technologies within specific industries. Such assistance, especially to small and medium-size manufacturing firms, maybe carried out through industry associations.

Although catching up with Western technology provided a clear goal for Japan through the 1970s, by the end of that decade this goal had been or soon would be reached in many areas. MITI's Next Generation program marked a shift toward an entrepreneurial approach to technology and economic development, supporting efforts far less certain of success. One account, from 1986, quotes a MITI technical official, lamenting reduced funding, as saying "the era of next-generation projects and grand projects is already over." Today, it appears MITI's role is far less significant than it once was and certainly quite different from that commonly believed in the United States.

SOURCES: Office of Technology Assessment, 1991, adapted from C. Johnson, ***MITI*** and ***the Japanese Miracle: The Growth of Industrial Policy, 1925-1975*** (Stanford, CA: Stanford University Press, 1982); ***Nihon Kogyo Shimbun***, "Follow MITI's Example," May 6, 1986, p. 3; L. Tyson and J. Zysman "Politics and Productivity: Developmental Strategy and Production Innovation in Japan," BRIE Working Paper No. 30, Berkeley Roundtable on the International Economy, Berkeley, CA, 1987.

tute (8). The rigid, noncompetitive nature of this research funding seems to limit the effectiveness of these expenditures (7,29).

In 1987, a general overhaul of Japan's universities was proposed by the Provisional Council for Educational Reform, appointed by Prime Minister Nakasone. Suggestions to change entrance requirements, encourage more international exchange, and foster creativity and individuality are still being studied (13). Anecdotal evidence suggests that some researchers have left universities for industry because of poor funding, inadequate equipment, and restrictive research environments wherein originality and creativity are not rewarded. University research contributes far less to the total research base of Japan than does university research in the United States.

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Ministry of Health and Welfare

In 1986, MHW established the Japan Health Sciences Foundation to promote biomedical and pharmaceutical research. Some observers feel this move was not only an attempt to meet Japan's growing health needs, made more pressing by a rapidly aging population, but also a response to MITI's biotechnology initiatives (30).

This foundation emphasizes small, cooperative R&D efforts involving companies, universities, and government institutes. Industry funds two-thirds of project costs. More than 100 firms, including several foreign fins, and approximately 400 researchers were involved by early 1990. Separate programs target biotechnology, medical materials, and immune mechanisms (12). In July 1989, Genentech received a small grant to study Werner syndrome, thus becoming the first U.S. firm to receive direct funding from MHW (2).

More significant to pharmaceutical companies are changes in Japanese drug pricing by the MHW national health insurance agency. Prices have been systematically lowered for older drugs, and new drugs are given premium pricing (see ch. 5 for further discussion of pricing). The result is pressure and incentive for greater innovation and higher R&D expenditures. These higher expenditures are forcing companies to seek larger markets, contributing to the continuing internationalization of Japanese pharmaceutical companies. The Japanese market for pharmaceuticals, on the other hand, is the world's second largest after the United States; Western companies, that have operated in Japan since World War II and new companies entering the world market directly are creating additional pressure on existing Japanese firms (48).

Science and Technology Agency

The Science and Technology Agency (STA) carries primary responsibility for funding basic research and coordinating basic science and technology expenditures. Similar to the situation with other independent agencies attached to the office of the Prime Minister, control of STA is fought over by other, more powerful agencies, such as, MITI and the Ministry of Education and Culture, which are responsible for staffing many positions (23). General policies are set by the Council for Science and Technology, chaired by the Prime Minister. The council has relied heavily on its advisory Policy Committee, consisting of senior industry executives. The council's influence is seen most directly in its Special Promotion Fund for Science and Technology, established in 1981 (49).

One project of interest was the human genome mapping and sequencing initiative, begun in 1981. This project focused on automating the sequencing process, with companies, such as Hitachi, Seiko, Fuji Film, Toyo Soda, and Mitsui Knowledge Industry, receiving funding from both the Special Promotion Fund and the Japan Research Development Corp. This frost-generation project, based on approaches quickly outdated by innovations in the United States, nevertheless caused considerable concern abroad. It was used by proponents of genome initiatives in the United States to generate public and private support for a human genome project in the United States. As in the United States, Japan's genome activities have been the subject of bureaucratic infighting and are controversial within Japan's scientific community. On the commercial front, Hitachi's second-generation sequencer had, as of early 1990, been made available only to Japanese Government scientists, and Applied Biosystems, a small California firm, remained the primary supplier of sequencers in Japan.

Another STA program is the System for Promotion of Exploratory Research for Advanced Technology (ERATO), established in 1981 to foster interdisciplinary, advanced research and technology. ERATO projects focus on technology development and are carried out in the private sector over 5-year periods by teams of about 15 scientists. Projects are funded by the Research Development Corp. of Japan (JRDC), a government-funded public corporation set up in 1961 to promote commercial use of government-developed technologies. Nearly half of the 14 current projects are relevant to biotechnology (20).

Ministry of Agriculture, Forestry, and Fisheries

In 1984, MAFF created a new Biotechnology Division, and the government declared biotechnology development to be the principal strategy for agricultural R&D (21). A basic research group made up of 14 firms was organized to carry out research. None of the firms was a traditional seed or nursery company, and many were participating in other biotechnology projects organized by other ministries (49). Private-sector research is further promoted by the Bio-oriented Technology Research

Advancement Institution, which provides up to 70 percent of finding for research projects and new ventures (21). Most of MAFF's 13 specialized research institutes and 6 regional experimental stations are involved in biotechnology-related research; the National Institute of Agrobiological Resources holds lead responsibility. The MAFF also funds university research (21).

Research Associations and Cooperative Research

In Japan, the typical cooperative project[1] is neither intensive nor high profile; although the large-scale integration semiconductor effort, mounted in the late 1970s, received much attention in the United States. It is touted by many as an example of how government-industry cooperation can forge technology breakthroughs (16). Most biotechnology-related projects in Japan are organized by government-sponsored research associations which coordinate modest projects carried out by researchers at member companies. According to some analysts, the participation of major Japanese companies in such projects has led outside observers to overestimate the project's importance. Cooperative research in Japan is thwarted by the same barriers found elsewhere: reluctance of the leading firms involved in the program to share information, difficulties over intellectual property rights, and, in the case of special research centers, failure of companies to supply their best scientists. Projects, therefore, tend to address potentially interesting but commercially low-priority targets.

An exception may be projects funded by Key Technology Center, which provides up to 70 percent of the cost of industry joint research projects. The center, which is a response to concerns about venture capital shortages for investment in emerging technologies, is largely financed by privatization of Nippon Telephone and Telegraph. The Protein Engineering Research Institute (PERI) project in Osaka will receive $150 million in government funding over a 10-year period. PERI, which involves 14 chemical, pharmaceutical, and food companies, has received a great deal of attention in the United States and Europe. Roughly 70 researchers are studying structure-function relationships with the ultimate goal, according to Katsura Morita of Takeda Chemical Industries, of fostering a strategic edge in protein engineering technology (28). Such research is critical to a number of important biotechnology applications. However, though the potential for PERI is great, to date there is little to show, which is not surprising since it is a long-term project.

Other officials point out the modest industry funding of most government-organized projects and suggest that companies take part in cooperative projects to get along with government ministries, but have little expectation of commercial return. At least one pharmaceutical company has refrained from participating in any Japan Health Sciences Foundation projects (organized by MHW) because managers believe it is better to concentrate on their own commercial research (43).

Research associations and cooperative projects can serve as a means to disseminate knowledge throughout an industry, a role played in the United States by an open university system and more flexible employment practices. However, lead companies (in Japan and in the United States) are often reluctant to share knowledge with competitors. Cooperative projects may have helped some firms acquire technical expertise. Their significance has shifted, however, with the commercial success and increased research intensity of Japanese industry and should not be overstated. There is no evidence that they have played a major role in the development of Japanese industrial biotechnology expertise.

Government-Industry Relations

Research and industry associations, along with numerous advisory groups, play an important part in a continuing dialogue between industry and government ministries. There is dynamic tension in the relationship between ministries and "their" industries. Formation of the Biotechnology Development Center (BIDEC) in 1982, under auspices of the Japan Association of Industrial Fermentation, was clearly a MITI initiative. MITI's influence is seen in BIDEC's activities, such as the organization of international conferences. It would, however, be wrong to assume that MITI controls companies in any way. MITI's current biotechnology plans are not greatly respected by many Japanese executives in biotechnology-related companies. MITI's influence depends on a variety of factors, not least of which is

[1]Cooperative research in this chapter refers to research involving three or more companies. It should not be confused with joint ventures, joint product development, contract R&D, or licensing agreements that typically involve only two firms.

the perceived quality of MITI's analysis, programs, and funding, and funding capabilities. Members of BIDEC use the association to influence policy to their advantage and tailor modest cooperative projects to their interests, if possible.

It now appears that Japanese industry is generally too successful and too powerful to be unwillingly guided into targeted investments. The power of the ministries may well have decreased with time. On the other hand, ministries such as MITI and MHW still have powerful regulatory roles. There are strong linkages between research and regulatory policies as is seen most clearly in MHW manipulation of drug prices to encourage innovation. When asked what policies most affect their companies, the overwhelming majority of Japanese executives interviewed by OTA in preparing this report named regulatory and pricing policies.

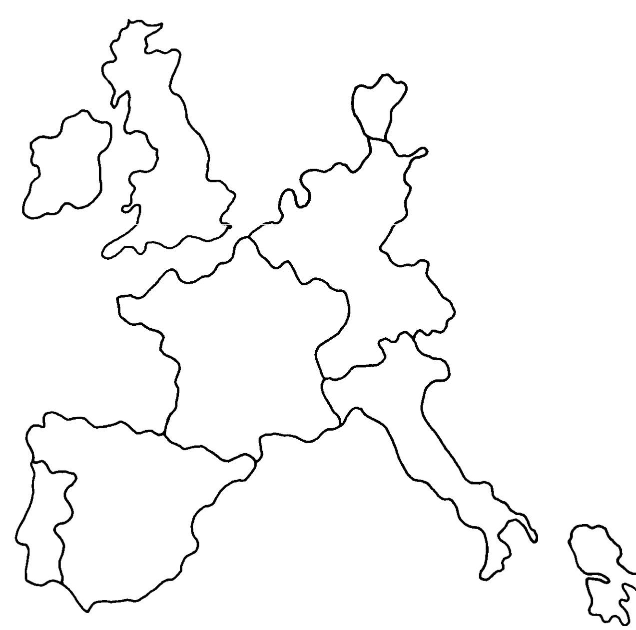
Conclusions

Japan's publicly funded basic research is weak when compared to U.S. efforts. Despite calls by the Science Council of Japan and recommendations in MITI white papers, the Ministry of Finance has not made funding increases. Initiatives such as PERI and the various ERATO projects, although significant, are still rare. Reform toward more creative and innovative research and training of creative and original thinking scientists in Japan's universities has only just begun.

Japan's strength is clearly in industrial R&D. The wide variety of companies attempting to utilize biotechnology in some way is impressive, from traditional sake and miso producers to Japan's largest multinationals. However, a number of companies, such as Kawasaki Steel, are pulling back from their biotechnology ventures (24). For such companies, diversification into biotechnology was a disappointment. Commercialization has taken longer, been more technically difficult, and been more dependent on factors unique to each industrial sector than expected. Biotechnology has not achieved the spectacular success that other fields have for Japanese industry.

Japanese high-profile, though modestly funded, industrial and research policies encouraged investment by a wide variety of companies. However, Japanese chemical companies were moving into higher value-added products, such as pharmaceuticals, prior to government initiatives. Japanese food processors have historically invested more heavily in R&D, compared to their counterparts in the United States and Europe. Japanese pharmaceutical companies now seem to view biotechnology in the same way as their counterparts abroad--i.e., as a powerful tool to supplement other research. Those companies, while more cautious than in the past, are continuing biotechnology research in terms of individual corporate strategies and assessments of commercial potential. For the foreseeable future, corporate strategies, rather than MITI initiatives, will likely determine Japan's investment in biotechnology.

Europe: Moving Toward a Regional Strategy?

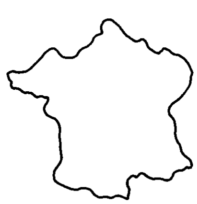


A number of European countries have technology policies that resemble those of the United States. National policies, however, are becoming less distinctive as Europe moves closer to economic integration. The effectiveness of national technology policies is limited by the evolution of an economically united European Community (EC) and, even more fundamentally, by the larger force of international competition.

If European national technology policies seem less significant than they were once thought to be, it is not yet clear that specific, regional policies for biotechnology-related fields will emerge. The research and commercial resources of EC countries, however, are enormous. Modest EC research programs currently underway aim to breakdown barriers to the effective utilization of those resources. Integration will also directly affect the non-EC European countries.

Each country promoting biotechnology illustrates a variation on how to promote science and technology of economic or strategic interest. The initial impetus may have been born in the government bureaucracy, in the academic community, or in industry. Where initial activities began, continue to influence how a country continues to pursue biotechnology R&D. Four European countries—France, the United Kingdom (U.K.), Germany, and Switzerland-are described in order to illustrate a variety of strategies. Regional programs, unique to Western Europe, offer yet another approach to strategic planning.

France: State-Initiated



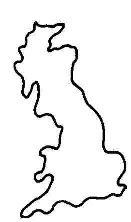
In 1979, the French Government responded to President Giscard d'Estaing's interest in ethanol fuels by producing a wide-ranging series of reports. The reports out-‘bed energy research as well as the potential for biology to change the relationship between humans and the environment, particularly in agriculture. The Mobilization Program, implemented in 1982, set for France the ambitious goal of achieving 10 percent of the world's biologically based production by 1990 (39).

Several research areas were targeted. Firms were to collaborate with various research institutes on a number of projects, and regional research and technology-transfer centers were to be established. Today, of the European nations, France is the leader in agricultural biotechnology. Biotechnology centers are well funded and staffed, and French seed companies have made major investments in biotechnology (41).

The French Government also attempted to reorient French researchers toward new biotechnology-related disciplines and more industrially relevant work. Unlike the situation in the United States, France's research strength lies not in its universities but in its government research institutes. Funding for all research, including research relevant to biotechnology, grew through 1985 but fell steadily after that. Still, new emphasis has been put on molecular biology, enzymology, immunology, plant genetics, and bioprocess engineering (42).

French planners thought that biotechnology would be essential to economic strength and national sovereignty. However, the various mechanisms established to achieve rather lofty goals have had limited success in areas other than agriculture and have been hampered by inconsistent government funding. France has had modest success in pharmaceutical applications of biotechnology-success that cannot be ascribed solely, if at all, to the Mobilization Program. While the large seed companies have invested in biotechnology R&D, the small and medium-sized firms, which make up the majority of the industry, continue to spend little on research (39). Of more significance now, may be regional policies. France is an enthusiastic participant in EC research programs and has pursued biotechnology through the French-inspired EUREKA initiative.

United Kingdom: Academic-Initiated

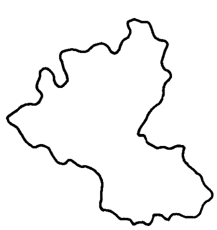


The United Kingdom most closely parallels the United States, with a strong research base, an emphasis on basic research (approximately 70 percent of government biotechnology funding), and a reluctance on the part of government to articulate a clear research or industrial policy. Britain does not have the advantages of scale available to the United States, and funding decisions have been difficult. The academic community, itself, was the force behind government initiatives, recommending a coordinated biotechnology policy to the reluctant, new Thatcher government in 1980 (39). But policy in the 1980's can best be described as "muddling through," with tight research budgets causing struggles among funding research councils, a situation exacerbated by modest initiatives for more industrially relevant, precompetitive research.

The most notable U.K. initiative has been the Biotechnology Directorate, established by the Science and Engineering Research Council in 1981. The research agenda, crafted by a steering committee of university scientists and industrialists, has moved steadily toward important biotechnology areas, such as protein engineering (38). In 1990, the United Kingdom formed a Biotechnology Joint Advisory Board, which is working toward coordinated research strategies between its various research councils (9).

British research is well-regarded and attractive to foreign, as well as British, companies. (Major British pharmaceutical and chemical fins, in fact, have been criticized for insufficient interest in the existing and available academic resources.) Many major foreign companies have established relationships with British institutions. Monsanto, for example, has a £20-million agreement with Oxford University. But poor salaries, combined with limited expectations for growth in research budgets, have caused a brain-drain of experienced researchers from the United Kingdom and a consequent crisis in recruitment that may make it difficult for Britain to maintain the quality of its science base (38).

Germany: Industry-Initiated

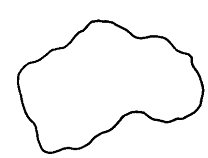


The 1974 creation of the world's first national biotechnology program, the German Society for Chemical Equipment, Chemical Technology and Biotechnology (DECHEMA) was backed by West Germany's large chemical and pharmaceutical companies and an effective trade association. Members were primarily interested in new fermentation techniques; it was not until the early 1980s that recombinant DNA (rDNA) and cell fusion were given equal treatment in targeted biotechnology spending by the Federal Ministry of Research and Technology (BMFT) (50). Nevertheless, today's reunified Germany has a strong, diverse base in underlying disciplines, a flexible and relatively diffuse research structure with substantial Federal and State support, and interactions between industry, universities, and research institutes that provide support to the country's strong group of large and medium-sized companies. Biotechnology techniques are well-integrated into those companies, and larger German firms have established research facilities in other EC countries, the United States, and Japan (37). However, Federal and State initiatives to encourage small biotechnology-based startup firms have had minimal success.

In August 1990, the German Federal Government approved a new biotechnology R&D program known as "Biotechnology 2000." The program's financial allocation for the period 1990 to 1994 is DME1.5 billion (approximately US$855 million). Although the program is designed to promote biotechnology research in the areas of the environment, public health, nutrition, energy, and natural resources pharmaceuticals will be a primary focus. As a result of Germany's reunification, biotechnology will also be promoted in what was formerly East Germany. Research institutes and businesses in the East will be eligible to apply for grants. It is expected that there will be active involvement in the program by industry (22).

German policies clearly arose from the private sector. They were built on an established research and educational infrastructure with less clear linkages to trade and regulatory policies. As discussed in chapter 11, acceptance of biotechnology by the German public remains problematic, and the German regulatory outlook is evolving.

Switzerland: Industry- and Academic-Initiated



Switzerland shares with Germany a strong emphasis on education and close ties between large Swiss chemical and pharmaceutical companies, such as Sandoz, Ciba-Geigy, and Hoffmann-LaRoche, as well as national universities and research institutes. Those ties, however, do not imply that universities emphasize developmental or applied research over fundamental science; firms support fundamental research at public institutions (19). Industry itself, carries out or funds around 75 percent of total country R&D. There is no formalized biotechnology strategy or articulated industrial policy. But Swiss industry, with its proven strength and willingness to develop and apply basic advances at Swiss or foreign laboratories and, typically, in foreign rather than Swiss production facilities, funds around 15 percent of university research-roughly three times more than industrial funding in the

United States (10). It is ironic that Swiss government incentives for industry participation in biotechnology research centers elsewhere in Europe may divert some research out of the country (19).

Regional Programs

The objectives of EC biotechnology programs (see box 10-C) are to mobilize the European research effort, target precompetitive research, and enhance the competitiveness of European industry. Several weaknesses are evident, however. Investment levels, for example, have been extremely low compared to other industrial areas. Altogether, the EC manages only about 3 percent of the community's total R&D expenditures; the rest are controlled by national governments (14) The new Biotechnological Research for Industrial Development and Growth in Europe (BRIDGE) program, which budgeted ECU 25 million (approximately US$30 million) per year from 1990 to 1993, is the most ambitious effort yet. It remains to be seen whether the program will maintain industrial relevance with high levels of industry participation. (Administrators hope that the new BRIDGE program will have greater industry participation.) Although most of these programs seek to stimulate participation by small and medium-size firms, this, to date, has not been the case.

Over time, however, the creation of regional research networks could enhance Europe's overall research capabilities and, through regional training and technology transfer, build the research capabilities of lagging countries. According to EC managers, the creation of various forms of translational cooperation, in and of itself, constitutes the main justification for the programs. The commission attempts to breakdown research barriers by connecting research centers (5).

Some observers fear that regional European research initiatives could provide European firms with advantages over their international competitors, thus aiding in the creation of "European champions. There is also concern that U.S. and Japanese scientists will be blocked from participating in European initiatives (l). In the short run, however, it seems likely that new regional biotechnology research initiatives will be less significant for industry than the regulatory, legal, and trade issues surrounding the drive to create a free internal European market by the end of 1992.

Mixed Messages

The proposed links between biotechnology research and other EC policy areas as of now are contradictory. European Community directives for contained use and deliberate release of genetically modified organisms, for example, have come under criticism from both promoters and critics of biotechnology. Despite the creation, in 1984, of a Biotechnology Steering Committee and establishment of the Concertation Unit for Biotechnology in Europe (CUBE) within the Directorate General for Science, Research, and Development (DG XXII), the very nature of biotechnology makes coordination difficult. Decisions having real, immediate impact on research investment and commercialization are driven by other concerns-e. g., policies on health, agriculture, and the environment-within the jurisdiction of separate Directorates-General (4).

The most striking contradiction in EC policy goals comes in the agriculture-food sector. Like U.S. farm programs, the Community's Common Agricultural Policy (CAP) has succeeded in easing the impact of technological change on the countryside. However, the price paid was surpluses, massive public expenditures, higher food prices, and, cumulatively, a hidden transfer of wealth from urban to rural regions. Biotechnology products that improve production yields, directly or indirectly (e.g., through improved animal health), run counter to CAP objectives. Suggestions that future animal health products show not only safety and efficacy but a positive socioeconomic impact might have a chilling effect on all new products, especially on biotechnology-related products (see ch. 11).

Continued debates on various directives needed to complete the internal market by 1992 reflect the rivalry among European interests. Outside observers should keep in mind the extent to which various directorates-general, themselves, represent distinct points of view or, as in the case of agriculture, are identified with a distinct political and economic group. The year 1992 is not so much a firm date as a process, and the creation of strategic policies at the regional level will be incremental before and after that date.

The United States: A Diffuse Approach

Japan's biotechnology fever in the early 1980s was in large part a response to the biotechnology boom in the United States. A series of startup

Box 10-C—European Biotechnology Programs

European Community (EC) Research Initiatives. European Community biotechnology research programs began with the Bimolecular Engineering Program (BEP). It dispensed ECU15 million (ECU1= @ US$l) in support of basic research from 1982 to 1986. Although funded by the EC commission, it was not a translational program. Rather, through competitive grants, BEP supported individual research groups performing isolated projects within the respective EC member countries. Funding amounted to 50 percent of project costs.

BEP was followed in 1986 by the 4-year Biotechnology Action program (BAP). This initiative differed from BEP in several ways. First, it focused on precompetitive research emphasizing the development of novel processes. Second, it supported translational cooperation by requiring more than one group from more than one EC member State participate in each project. Third, through its training stimulation scheme, it encouraged scientists to work in other EC laboratories outside their native countries. Finally, it enjoyed a generous annual budget of ECU13.75 million per year.

Under BAP, expenditures continued to cover 50 percent of the cost for R&D ventures. Roughly 123 projects, involving 413 laboratories, were funded. France and the United Kingdom were the largest beneficiaries, each receiving roughly 18 percent of total dispersals through BAP's competitive granting scheme. Portugal received the smallest share, acquiring 2 percent of the cumulative expenditure.

BAP's emphasis on translational activities gave birth to the concept of "laboratories without walls," whereby scientific organizations from various EC counties participate in joint research projects. One such project, the lactic acid bacteria cluster, links Ireland, the United Kingdom, The Netherlands, and Germany in R&D projects focusing on gene cloning systems, efficient gene expression, protein secretion, plasma replication, and the improvement of various starter cultures. These efforts encourage the exchange of information, technology, materials, and staff; they are designed to eliminate bottlenecks within the scientific community. As research matures, the efforts may take on independent lives, e.g., spawning more applied research or proprietary relationships between participating laboratories, scientists, and industry.

The Biotechnological Research for Industrial Development and Growth in Europe program (BRIDGE) is planned for 1990 through 1993. Its research areas include the information infrastructure, enabling technologies, and cellular biology. Its 5-year budget will total ECU1OO million, at ECU20 million per year. Support will continue to be awarded on a competitive basis and, like the BAP, will cover 50 percent of R&D costs.

BRIDGE's objectives are to further strengthen industrial applications of biotechnology and to enhance translational research. To this end, it will incorporate projects that focus on providing a link between basic and applied research. A minimum of 10 to 20 laboratories will participate jointly in these ventures. Annual expenditures are expected to run ECU1 million to ECU3 million per project per year.

companies, founded in the United States in the late 1970s and 1980s, commercialized research breakthroughs. Nearly 70 new firms were begun in 1981 alone (45). Companies such as Genentech went public and were able to raise substantial amounts of cash (see ch. 4). Established chemical, pharmaceutical, and seed companies entered into research agreements with the new firms, established biotechnology research groups, or acquired startup fins. First entry of products created by rDNA technology fed expectations of near-term revolutionary changes in the pharmaceutical industry and other sectors, that now seem premature.

In Japan, relevant policymaking is dominated by tension between competing bureaucracies and powerful industries. In the United States, policymaking is driven by the dynamics of interest-group politics. Although Japan is far from monolithic, the sheer number of actors in the United States makes achieving consensus and continuity much more difficult. Pluralism is reflected throughout the political process of budgeting and appropriating funds. Although business interests play a strong role in this process, they are not as dominant as in Japan (see app. B). Congress plays a far stronger role in funding and oversight than does the Japanese Diet, and executive agencies have markedly less discretion or authority than their counterparts in Japan.

The structure of the U.S. research and technology base is, also, vastly different. As noted previously, the Federal Government provides, in both relative and absolute amounts, significantly more funding than does the government of Japan; and a much higher percentage of nondefense R&D goes to basic research (see box 1O-D). The U.S. Government funds roughly half of the Nation's total R&D, and

One project of particular interest will concentrate on sequencing the yeast genome and will involve 28 laboratories throughout the EC. The total EC contribution to this project should reach ECU8 million. A second initiative will focus on the molecular identification of new plant genes. The EC investment in this effort will come to ECU5 million.

Two EC agricultural programs support biotechnology research. European Collaborative Linkage of Agriculture and Industry through Research (ECLAIR) has a 4-year budget of ECU80 million and aims at improving the integration of farm activities with upstream (supply) and downstream (processing) industries. The related Food-Linked Agro-Industrial Research (FLAIR) program will run through 1993; it is aimed at improving food quality, safety, and diversity-rather than agricultural productivity. Funding is ECU25 million.

EUREKA. EUREKA (European Research Coordination Agency) was originally created in 1985, allegedly in response to the U.S. Strategic Defense Initiative (SDI). It has since evolved into a coordinating agency linking advanced technology projects being carried out by European industry. EUREKA projects are not limited to EC countries, and also include Norway, Sweden, Finland, Switzerland, Austria, Iceland, and Turkey.

Project area	Number of projects	Participating companies and labs	Approved budget (in million ECUs)
Agro-Food	3	6	5.4
Agronomy and aqua culture	9	27	55.7
Biochemical engineering and cell culture	8	25	124.2
Biomedical engineering	7	18	55.2
Human health	12	28	88.9
Protein design	1	3	16

SOURCE: *Biofutur* (Biofutur, April 1989).

Although biology was not an initial priority, as of mid-1989 EUREKA had approximately40 biotechnology, food, and biomedical projects (of over 210 total projects). They areas follows:

Although the EUREKA's focus on commercially significant research and translational industry cooperation could have more immediate impact than the EC programs, it is still too early to evaluate its effectiveness. Public funding for EUREKA projects has been less than anticipated, and the most recent approvals may not reach 50 percent.

SOURCE: Office of Technology Assessment, 1991, adapted from E. Magnien et. al., "Les Laboratoires Europ ens saris Murs," *Biofutur*," R. van der Meer, "*Biotechnology in the Netherlands*"; paper presented at OTA international conference on Biotechnology in a Global Economy, vol. S4, November 1989, pp. 17-29.

OTA estimates that the Federal Government funds more than half of total biotechnology-related research (45). The United States has a decentralized research system, and several cabinet-level departments have internal research divisions responsible for the research needs of their particular missions, such as enhancing health (46).

The system for setting research budgets in the United States is inherently political. Constituencies advise agencies informally and through official advisory boards and committees. The constituencies support their own spending priorities during the budget and appropriations process. The role of Federal agencies is crucial to the success of Federal research efforts, as the agencies are intricately involved in the day-to-day operations of the research system. Each agency has its own culture. These cultures contribute to their success, perhaps simply by embodying the way things are done. ' However, the cultures are powerful determinants of future directions, and specific goals may only be reflected in the collective knowledge of agency personnel (46).

Overall Funding Trends for Biotechnology

Historically, the United States, both in absolute dollar amounts and as a percentage of its research budget, has had the largest commitment to basic research in biological sciences worldwide. In 1988, OTA found that 12 Federal agencies and one cross-agency program, the Small Business Innovation Research Program (SBIR), spend research dollars on biotechnology (45). The National Institutes of Health (NIH) funds nearly 85 percent of all federally funded biotechnology, thus playing the

Box 10-D—United States Support of R&D

In 1990, the United States spent an estimated $150 billion on research and development (R&D). This represents an annual real increase (in constant dollars) of 1.3 percent-the 15th consecutive year in which the national R&D effort grew faster than inflation. This extraordinary record was comprised of a period of consistent growth above inflation in the late 1970s and early 1980s, then a short spurt of tremendous growth in the mid-1980s, and over the past few years, a shift toward modest growth rates--around 1 percent above the inflation rate.

The United States devotes more resources to supporting R&D than any nation in the world. The estimated $150 billion to be spent in fiscal year 1990 is more money than the combined R&D spending of Japan, Germany, the United Kingdom, and France. As a percentage of Gross National Product (GNP), however, the United States is not so dominant. Over the past 20 years the United States has consistently spent a larger share of its GNP on R&D than some nations (like the United Kingdom and France), but since the late 1970s, West Germany and Japan have increased their R&D/GNP ratios considerably. By 1988, these two nations and the United States were spending between 2.7 and 2.9 percent of their respective GNPs. In 1990, the estimated R&D effort in the United States of $150 billion represents 2.7 percent of the American GNP. This ratio is up from the 1971 low of 2.1 percent (which followed cuts in defense and space programs), and it is just shy of the peak level of 2.9 percent achieved in 1964. Considering only nondefense R&D spending, however, the situation is somewhat different. While the ratio of nondefense R&D to GNP in the United States is still larger than the United Kingdom and France, Japan and Germany have much higher ratios, these have been consistently higher than the U.S. ratio over the past 20 years.

The national R&D effort is shouldered primarily by the Federal Government, industry, and academic institutions. In 1990, industry and the Federal Government together accounted for nearly 96 percent of total support, with universities and colleges contributing 3 percent, and other nonprofit institutions funding 1 percent. Today, industry is the largest single source of R&D funds, providing $74 billion compared to the Federal Government's $69 billion. The past decade represents a period of great growth in industrial R&D spending, as only since 1980 has industry spent more than the Federal Government on R&D.

SOURCE: Office of Technology Assessment, *Federally FundedResearch: Decisions For A Decade,* 1991,

special role described below. The other agency programs are described in appendix C.

The National Institutes of Health—The NIH is the largest research agency in dollars awarded to basic and applied research in the Federal Government. Of fiscal year 1990's appropriation to NIH, $2.9 billion was biotechnology-related. NIH is the principal biomedical research arm of the Department of Health and Human Services (DHHS), and it funds biomedical and basic research related to a broad spectrum of diseases and health problems in both its own research facilities and at outside organizations. The NIH has been the principal funding source for biotechnology across all fields. But should, or can NIH continue this role? This is not a new question; in 1984 and 1985, considerable public discussion on the role of NIH took place between the President's Science Adviser, George Keyworth, and NIH Director, James Wyngaarden. Keyworth pushed for a broader NIH role in meeting nonmedical biotechnology needs, while Wyngaarden resisted this expanded NIH role (6). At a 1985 NIH Advisory Committee conference, some consensus was reached on the need for expanded, interdisciplinary training for biotechnology, but calls for an expanded role in more applied or intermediate research were resisted (47). At the time, concerns about the effect of more targeted research on basic research funding were expressed, with industry coming to the aid of academic science in supporting the importance of NIH's commitment to funding basic science. More recently, parts of the scientific community balked at the prospect of an ambitious effort to map and sequence the human genome, fearing that such directed research detracts and subtracts from resources for fundamental research.

These concerns not only remain pertinent but also have become more acute in light of budget constraints. Despite real growth over the last decade, NIH views itself as being in a steady state and finds itself under strain. With biotechnology increasingly integrating into other research fields, and with budget pressures building, it will be difficult for NIH to support biotechnology across all fields. Until 1990, scientists in plant and animal science, who have relied on NIH for funds because there have been no other sources, were fearful that budget constraints could imperil their only source of funding as NIH eliminates or cuts back on projects not central to its mission (51). But the 1990 Farm Bill and the 1991 U.S. Department of Agriculture (USDA) budget showed major increases for competitive grants in these areas.

From the Laboratory to the Market

University-based research was the foundation of U.S. leadership in initial commercial applications of biotechnology. Indeed, biotechnology in the United States is, in many respects, an example of successful technology transfer. Venture-funded startup firms first brought advances in the biological sciences into the commercial arena in the 1970s; today, university researchers often move easily between academic and commercial pursuits. Universities themselves are seeking more financial returns from the products of their intellectual capital. This is not a surprising phenomenon, given the closeness between biological research and application.

Recent trends in the biological sciences indicate a move away from broad, lengthy agreements between universities and industry and toward numerous specific agreements. Genentech, until 1990 one of the largest and most visible independent biotechnology-based pharmaceutical companies, may have up to 500 active agreements at any one time (15). Agreements such as the one between Monsanto and Washington University (initiated in 1982 and scheduled to run through 1994, involving over $100 million) are the exception, not the rule.

Extensive university-industry ties in the biological sciences have highlighted concerns common to a number of fields. Some critics wonder if Congress and the executive branch have gone too far in encouraging the commercial exploitation of university research. Recent congressional hearings have focused on personal and institutional conflicts of interest--questioning whether the integrity of university or government laboratory research has been compromised by allowing private gain from public investment. Critics of aggressive technology transfer out of the universities have asked whether scientists with a substantial financial stake in research outcomes can be objective in reporting research results. These questions, mentioned in an earlier OTA report (45), remain largely unresolved. In response to these criticisms, however, universities and professional journals have developed disclosure guidelines for making public the personal and financial interests of researchers. Until recently, such disclosure was strongly resisted (15). The NIH responded to mounting concern by proposing, in September 1989, guidelines for university researchers receiving Federal funds. Industry opposed the initial guidelines, which were withdrawn in December 1989, as a threat to commercialization of university biological research. In addition, the 1990 Farm Bill contains a provision that requires land-grant universities to establish conflict of interest policies.

Subtle questions are raised as universities attempt to profit from research relationships. Are the factors that make such relationships attractive-including an atmosphere fostering innovation through the free and easy flow of ideas--threatened by agreements that are overly protective of a university's financial interests? Also, should U.S. academic institutions—encouraged by congressional, executive branch, and State actions to license technology-be criticized when the licensee is foreign, even when U.S. firms expressed no interest in the technology?

Consortia, Centers, and Cooperative Research

In recent years, the U.S. science community has engaged in an ongoing debate over the appropriate size and organization of research efforts-particularly in the life sciences. Proponents of more directed research criticize the traditional investigator-initiated, individually funded approach typical of federally funded biomedical research (3). The biological sciences remain, for the most part, wedded to this approach, although other disciplines have come to rely more on fewer, but more expensive, facilities and larger research teams (the so-called "big science' '). Some argue that the interdisciplinary nature of modern biological research requires a shift toward big science. Others suggest that efforts requiring large amounts of time-consuming, repetitive work, such as mapping and sequencing the human genome, would be best carried out in centralized facilities with large data-handling capabilities. Flexibility has been urged by many, who point out that different approaches could be necessary for different types of research. A larger critical mass of researchers might be appropriate for some types of generic, applied, or intermediate work; and individuals or small teams might be more likely to generate both basic innovations and specific applications.

A more concentrated approach could be desirable for certain bottleneck areas of basic or applied research. Although some advocate the establishment of industrial consortia to achieve those purposes (26), others argue that because so much of commercial significance comes out of basic research itself, cooperative research on a large scale is difficult if not impossible (27). In fact, some believe that innovative new companies may have little to gain from participating in consortia with larger but less innovative companies (34).

In 1987, an effort to create an industry-based consortium for protein engineering research in the United States failed. Although supported by researchers at a number of U.S. companies, participants say that upper management was concerned about consortium funding and the sharing of information coming out of joint research (11).

Consortia have been touted by some as a cure-all for the perceived weaknesses of U.S. high-technology industries (36). In the United States, cooperative research usually takes the form of a "center" that is mostly university-or government laboratory-based, low profile, and modestly funded. The primary function is to provide companies with a window on new technology and access to research conducted at the center. A center may also give companies access to personnel. These consortia or centers are typically organized by enterprising university or government laboratory entrepreneurs, who utilize public funds as an incentive for private investment in university or government laboratory biotechnology centers. Frequently, centers are part of State or local economic development efforts (45). An exception to this is the Midwest Plant Biotechnology Consortium (MPBC) involving 12 States, over 15 universities, 3 Federal laboratories, and nearly 40 agribusiness corporations. The MPBC carries out research in plant biotechnology, encompassing Midwestern crops and cropping practices.

Universities have attempted to provide a forum where companies can truly cooperate in precompetitive research. However, frequently, little cooperative research occurs and, instead, a series of agreements develop between university management and individual companies. Any cooperative work is financed through a general membership fee paid by industrial participants, few of which have much riding on the outcome of such projects. Membership takes many forms, sometimes as industrial liaison programs. One executive of a large chemical company said that his firm participates in a number of university-based consortia, but that in most cases it is token participation through payment of a small annual fee. Smaller companies may find even a small fee prohibitive. Companies may feel such participation is good for public relations, but have little expectation for tangible benefits. On the other hand, a few projects are quite serious; in general, they involve fewer industrial partners, who have specific expectations and are contributing significant amounts of money (33).

Although several limited consortia have been formed in biotechnology, broad-based consortia in biotechnology are not likely to emerge unless there are clear technical advantages that cannot be easily solved by companies working alone, a strong challenge is posed by foreign industry, or government funding is provided as an incentive to cooperation. Otherwise, cooperative initiatives are likely be the exception, not the rule, and large-scale projects few in number.

NATIONAL POLICIES IN A GLOBAL ENVIRONMENT

What is the national interest in a global research and commercial environment? This question is becoming more difficult for national governments to answer. National interests affect decisions on research priorities, training programs, and relationships between universities and research institutes with domestic and foreign fins.

In general, U.S. policy toward nonmilitary R&D has been to support basic research, with the expectation that industry will develop and apply that research in the marketplace. United States priorities, however, are brought into question by the commercial success of companies in countries such as Japan, that benefit from a greater emphasis in government-funded programs on applied research and technology than on basic science. The one exception maybe U.S. biotechnology, which has grown out of the large federally funded biomedical research base.

For several promising application areas, especially human health, agriculture, and environmental protection, certain applications of biotechnology have the potential to address social needs. To some, this role indicates a moral imperative to advance knowledge, regardless of political borders or economic issues. This is especially an issue for the United States, which spends significantly more than other countries on biomedical research. Judging by citations in published scientific articles, biomedical research is markedly international (46). Few scientists would support limits on communication and collaboration. Many would argue that the volume and extent of information flows, regardless of borders, have greatly speeded the advance of knowledge.

In addition, there is common interest in establishing new, international databases for research and regulatory purposes and in developing appropriate technologies for the Third World. Scientists in a number of countries are exploring ways to cooperate on mapping and sequencing the human genome. Threats by the United States to limit access to U.S. prepublication results have caused concern at home and abroad. Such restrictions would have a greater effect on small foreign companies than on multinationals with U.S. operations (18).

Domestic University-Foreign Industry Relations

Restricting foreign access to, and funding of, domestic research might be feasible if a country has the following:

- a clear technology lead,
- firms that have little to gain by similar access abroad,
- domestic companies supporting domestic research and licensing available technology, and
- a clear distinction between domestic and foreign firms.

These conditions, however, seldom apply.

The United States may have a clear advantage in many areas of biomedical research, but it may not have such an advantage in other fields where biotechniques are being developed. Significant work is also carried out in foreign institutions in almost all areas, and U.S.-based firms have established relationships with foreign universities and research institutes. Monsanto's arrangement with Oxford University has already been mentioned. Calgene has licensing and technology-transfer agreements with universities in Canada, France, Japan, and the United Kingdom. Mycogen has agreements with Japanese and European firms. Genentech received a small grant from the Japanese MHW for cooperative research on premature aging, and also has several agreements with Japanese universities. United States and European pharmaceutical firms have established research facilities in Japan.

There are a number of long-term agreements between foreign firms and U.S. universities. Hitachi is building a new research facility at the University of California-Irvine that will become fully owned by the university in 30 years. Several European firms have established research facilities in the United States and fired university research in this country.

Under the pressure of international competition, companies are obliged to take advantage of innovation quickly-regardless of origin. According to one observer: "Both multinational corporations and new biotechnology firms choose their academic partners irrespective of national borders" (17). Some U.S. industry and university observers feel that the real question is not why U.S. universities are doing business with foreign companies, but rather, why more U.S. firms are not taking full advantage of U.S. universities.

Some university administrators also point out that U.S. firms, themselves, frequently license technology to and from foreign countries. Such agreements reflect the financing needs and marketing strategies of small and large firms. This situation raises the underlying question of national interest in a global, commercial environment. Is funding for U.S. research to be rejected because it comes from a foreign-based company? Will access to publicly funded research be restricted to U.S. firms that may license products abroad or carry out substantial research or commercial activities abroad? United States law requires inventions developed with Federal funds to be manufactured domestically for U.S. markets (Public Law 96-517).

Basic research's significance for current biotechnology products makes these questions more difficult to answer, as do the different roles and degrees of access to universities in various countries. Research in Japanese universities, for example, is not comparable to that in the United States. Some people in industry say that advocates of an open, international research and commercial environment are naive, and that the only way to have any success is to keep new and important technology stateside (32). However, other industry observers say that science is a lousy place to say "buy American" (40).

SUMMARY

When recombinant DNA and cell fusion techniques were developed during the 1970s, the potential of biotechnology excited scientists, industrialists, and government officials. But, as with other profound advances in knowledge, developments have confounded the predictions and expectations of even the best/informed observers. In some ways, early commercialization of proteins, derived from genetically modified organisms, fed expectations of scientists, financiers, business people, and, not least, government officials. The expectations were unrealistic. Biotechnology may prove to be the last great revolution in knowledge in the 20th century and a significant underlying technology for the 21st century, but its full impact has not yet been felt.

Many governments, enamored by biotechnology's potential and concerned that their domestic industry not lose out in developing anew field, have launched specific biotechnology development efforts. Governments everywhere are realizing that high-technology helps drive industrial competitiveness and economic strength. For many, biotechnology became a test case, not only at the national level, but in many States (i.e., North Carolina, Maryland, and Massachusetts).

Many components of such strategies, such as: the emphasis on technology transfer, development of incubator facilities and venture capital for startup fins, and establishment of interdisciplinary centers for research are certainly helpful for focusing attention. However, in a sense, they operate at the margins. In 1984, OTA found that government expenditures on research (and the concomitant development of trained scientists) were among the most significant factors influencing competitiveness in biotechnology. A strong research base is the first priority allowing small companies and venture capitalists the opportunity to take risks. Without this, industry-oriented programs will not be very successful. Observers concerned about Japan may note that Japan is now working hard to train scientists although spending on basic research still lags, as compared to the United States.

If targeted biotechnology strategies have been largely unsuccessful, some of the reason may be because of the way biotechnology arose out of basic biomedical research, only to become fully integrated into the various fields of life sciences. The term biotechnology retains coherence only to the extent that regulations, public perceptions, and intellectual property law deal with specific biotechnology techniques as something unique.

The challenge, then, for national governments is to sort out national from private interests. A task that will become more difficult as competitiveness is used as a justification for particular expenditures. For the most part, political support of research in this country is based on perceived social needs—fear of disease, concern for an adequate food supply or the environment, and national defense. Economic nationalism may be particularly difficult to define and pursue, given the pluralistic, incremental, and increasingly global nature of the world's R&D system.

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