Chapter 13

# Government Funding of Basic and Applied Research

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## Introduction

Federally funded basic research in the United States has been essential to the development of biotechnology. The United States currently has a strong and diversified basic research capability, the foundation for which was laid during World War 11 by the Office of Scientific Research and Development (OSRD). The National Institutes of Health (NIH) was established to succeed OSRD'S Committee on Medical Research in 1930.

Within a few years after World War H, several patterns of U.S. Government funding for basic research had been established. First, funding of scientific research would further the broad aims and priorities of the U.S. Government as defined by Congress and the President. Second, nongovernmental laboratories (e.g., research universities) would perform much of the research of interest to the Federal Government; in-house Government laboratories would also perform such research, Third, direct relationships between Federal agencies and university researchers would be established; funds for university research would be awarded to individual investigators or small teams of investigators rather than to the institutions themselves (legally, funds are administered through institutions in the name of investigators). Fourth, university research and graduate training in the United States would be closely related functions. These patterns, with elaboration, have persisted until the present (21).

The launching of Sputnik in 1957 triggered a spectacular increase in the U.S. research effort. From 1953 to 1967, national expenditures in current dollars for research and development (R&D) increased by more than 350 percent, and current dollar R&D expenditures by the Federal Government increased almost 425 percent, In 1967, Federal Government expenditures represented 62 percent of total national expenditures for R&D. After 1967, the rate of growth in R&D expenditures declined, and by 1976, the Federal Government's contribution had dropped to an estimated 53 percent of total national R&D expenditures (21).

National basic research expenditures by the Federal Government have decreased more sharply in constant dollars than in total R&D outlays. Between 1968 and 1976, basic research expenditures declined in constant dollars by an estimated 15 percent. Since universities perform the greatest share of basic research, they have suffered the most from constraints on Federal research funding. In real dollars, fewer basic research funds were spent in universities in 1976 than in 1968 (21). In spite of this leveling off of Federal support, the basic research effort of the United States is prodigious and led to the recent developments in biotechnology.

one aspect of the development of biotechnology demonstrates the unanticipated results of a long-term commitment by the U.S. Federal Government to basic research. The "war on cancer" stimulated investigators to study the properties of viruses that cause tumors. * A great deal of work was done to locate the genes in several tumor viruses, such as SV40 virus, that cause tumors in hamsters and mice. These viruses are particularly recalcitrant to classical genetic procedures for mapping genes. This problem led to the use of bacterial restriction enzymes-enzymes that cut DNA at specific locations—to construct physical maps of genes. Physical mapping of an entire genome (a complete set of genes of an organism) using restriction enzymes was first accomplished on SV40 DNA. It was the knowledge of the mechanism of action of these ***restriction*** enzymes, generated originally from cancer research, that led to the cloning of genes.

*See *Appendix C: A Comparison of the U.S. Semiconductor Industry and Biotechnology*.

As biotechnology is commercialized, different emphases will be placed on various aspects of the continuum that stretches from basic to applied research. The objective of basic research is to gain a better understanding of the fundamental aspects of phenomena without goals toward the development of specific processes or products, The objective of applied research is to gain the understanding necessary to meet a recognized and specific need, process, or product (13). Bridging the gap between basic and applied research is "generic applied" research, which is more specific than basic research, but longer term and more risky than most applied research. * The Federal commitment to basic and generic applied research in the United States will be a necessary element in the commercialization of biotechnology in the coming years.

Donald Kennedy has characterized the process that moves from basic, to generic applied, to applied research as the "trajectory of innovation" (10). Within this trajectory, particular kinds of institutional sponsors play defined roles:

- Phase ***One*** (Basic Research). Characterized by loose, informal organization, open communication, quick publication of all the details of an experiment. Usually takes place in university departments or laboratories such as those at NIH, or sometimes in a special organization such as Bell Laboratories. Most often publicly funded, oriented toward the discovery and explanation of phenomena.
- Phase Two (Generic Applied Research). Focused on processes, the application phase. Takes place in various settings: applied institutes, some university departments, nonprofit organizations (e.g., Stanford Research Institute, Battelle). Mixed public and private funding. Environments variable with respect to proprietary secrecy.
- ***Phase Three*** (Applied Research). Innovative emphasis on products, the development stage, attention given to practical application. Funding by private risk capital, environment tends to be closed for proprietary reasons, essentially all work takes place in private laboratories.

Biotechnology is moving rapidly along the trajectory of innovation. The role of Federal funding in the process has been and will continue to be critical to the U.S. competitive position in biotechnology.

Assessing the US. competitive position in biotechnology research is difficult for several reasons, First, the definition of biotechnology used in this report is a definition specific to the commercialization of biotechnology, and thus is more likely to fit traditional definitions of applied research. Second, basic or fundamental research in biotechnology can include research on topics as diverse as cancer, developing new vectors to improve recombinant DNA (rDNA) techniques, increasing oxygen volubility in aqueous systems, understanding immune function, and neurobiology. Basic research by its very nature is wide ranging; many elements drawn from basic research of various kinds go into the innovation and development of a particular patentable product. Third, the use of rDNA techniques or rDNA research may be but a small component of a particular research project, or the description of the particular research may not have contained key words that warranted its inclusion in an agency classification of biotechnology research. In addition, as rDNA techniques are more widely used, much of basic research at the cellular and subcellular level will use these techniques; thus, much of basic biomedical research will use the techniques of biotechnology, Fourth, even in the United States, biotechnology is defined differently among funding agencies. Added to problems of definitions are differences in granting procedures by various agencies, as well as different accounting procedures for indirect costs (indirect costs are part of the cost of doing research and therefore must be included). And, finally, overall funding levels give some indication of the total research effort but do not reveal the quality of the research. Nevertheless, most experts would agree

● Generic applied research is a part of the continuum between the two poles of basic and applied. This research may be characterized as follows: 1) it is not committed to open-ended expansion of knowledge as university basic research typically is, but is less specific (more widely applicable or "generic") than the typical industrial product or process development effort; 2) it has more well-defined objectives than basic research, but is longer term than typical product and process development efforts; and 3) it is high risk, in the sense that the stated objectives may fail and the resources committed may be lost for practical purposes.

that the two are closely correlated and that the United States leads the world both in its investment in science and in the quality of its science. The totals for Federal funding for biotechnology research are shown in table 56 and will be discussed in the sections to follow.

Since the focus of this chapter is an assessment of the relative strengths of basic, generic applied, and applied research in biotechnology in the United States, Japan, the Federal Republic of Germany, the United Kingdom, Switzerland and France, the estimates of government funding for biotechnology research in other countries that are available have been included in this chapter. Given problems with respect to definitions, currency exchange fluctuations, and lack of complete data, these figures must be interpreted with caution. For detailed analysis of agency budgets within the United States, the reader is referred to the American Association for the Advancement of Science and National Science Foundation (NSF) documents listed in the references (1,13).

The three sections of this chapter that follow are intended to provide a perspective on the U.S. commitment to biotechnology research by discussing basic, generic applied, and applied biotechnology research, respectively, within individual U.S. Government agencies. A separate section considers instrumentation initiatives by the U.S. Government that have bearing on biotechnology research. Near the end of the chapter, research expenditures in biotechnology and channels of research funding in Japan, the Federal Republic of Germany, the United Kingdom, Switzerland, and France are presented in a comparative overview. The final section of the chapter identifies issues and congressional policy options pertaining to U.S. Government funding of biotechnology research and instrumentation initiatives.

**Table 56.—U.S. Federally Funded Research in Biotechnology[a]**

| | | Amount of funding (millions of dollars) | | |
|---|---|---|---|---|
| | | Basic | Generic applied | Applied |
| NIH: | | | | |
| Molecular biology, generic manipulation, hybridoma, monoclinal antibodies | FY 1982 | $378.0 | | — |
| Immobilized enzymes | FY 1982 | — | $ ; 0 | — |
| NSF: | | | | |
| rDNA research | FY 1982 | 12.8 | — | — |
| Bioprocess engineering | FY 1982 | — | 1.7 | — |
| Other biotechnology-related research (broadly defined) | | 38.6 | — | — |
| USDA: | | | | |
| ARS plant biotechnology | FY 1983 | 7.2[b] | — | — |
| ARS animal biotechnology | FY 1983 | 6.4[b] | — | — |
| CSRS competitive grants (CRGO) | FY 1982 | 5.0 | — | — |
| SAES | 1981-82 | 15.6[b] | — | — |
| DOD: | | | | |
| DARPA | FY1983 | | 2.2 | — |
| Army/Navy/Air Force rDNA research | FY 1983 | 3 ; | — | — |
| Other biotechnology | FY 1983 | 2,0 | — | — |
| DOE: | | | | |
| Photosynthesis, stress mechanisms of plants and micro-organisms, genetic mechanisms, methanogenesis, etc.[c] | FY 1983 | 9.9[b] | — | — |
| Conservation & Renewable Energy Program | FY 1983 | 23.7[b] | — | — |
| Other | FY 1983 | 2.0[b] | — | — |
| Biocatalysis research | FY 1983 | — | 0.5 | — |
| Total | | $510.9 | $6.4 | $5. O(SBIR) |

[a]Unless otherwise specifled, see text for explanation of figures
[b]Some of this research may be generic applied research
[c]Biotechnology, broadly defined

SOURCE Office of Technology Assessment

# U.S. Government funding of basic research in biotechnology

U.S Government agencies funding basic research in biotechnology are NIH, NSF, the U.S. Department of Agriculture (USDA), the Department of Energy (DOE), and the Department of Defense (DOD).

## National Institutes of Health

In November 1983, the fiscal year 1984 budget of NIH **was** appropriated **at** $4.3 billion with some of the unauthorized programs still under continuing resolution. The number of new and competing project grants will be maintained at 5,000. * The 16)560 research project grants—5)000 competing and 11,560 noncompeting-will be the largest number of research project grants supported in the history of NIH. Budget estimates indicate that direct costs for noncompeting continuation grants will be reduced by about 1 to 2 percent and those for competing grants by 2 to 4 percent. A 4-percent reduction in average costs was applied to these grants in both 1982 and 1983,

Most of the basic research that has been and is done in biotechnology is NIH-funded research. Despite the budget pressures on NIH funding as a whole, the number of extramural projects using rDNA techniques has increased, Funding figures for NIH projects in biotechnology for the fiscal years 1978 to 1982 are shown in table 57. Since data are cataloged by NIH staff on the basis of grant applications or progress reports and indexed by staff who looked for key words such as “genetic manipulation,” “hybridoma)” “monoclinal antibodies,” and “immobilized enzymes, ” the figures may be slightly misleading. For example, the term “genetic manipulation” includes some projects that do not involve rDNA techniques. Also, the figures are the total costs associated with the awards, including direct and indirect costs, and are not related to the proportion of rDNA research in the total research effort. With the exception of generic applied research on immobilized enzymes, the work is primarily basic research, so many of the industrial applications associated with new biotechnology may be in the distant future. Despite these classification problems, it is evident from the figures in table 57 that research using rDNA techniques is becoming more widespread and comprises a larger proportion of the total grants awarded each year.

**Table 57.—NIH Projects in Biotechnology, Fiscal Years 1978=82**

| Fiscal year | Number of projects | Dollars awarded (millions of dollars) |
|---|---|---|
| *Genetic manlpulatlon:* | | |
| *1978* . . . . . . . . . . . . | *546* | *$61* |
| *1979* . . . . . . . . . . . . | *847* | *103* |
| *1980* . . . . . . . . . . . . | 1,061 | 131 |
| 1981 . . . . . . . . . . . . | 1,400 | 164 |
| 1982 . . . . . . . . . . . . | 1,588 | 185 |
| *Hybr!domas (term not created until 19/?0):* | | |
| *1980* . . . . . . . . . . . . | *256* | *$ 22’* |
| *1981* . . . . . . . . . . . . | *479* | *49* |
| *1982* . . . . . . . . . . . . | *654* | *64* |
| *Monoclinal antibodies (term not created until 1980):* | | |
| *1980* . . . . . . . . . . . . | *268* | *$22* |
| 1981 . . . . . . . . . . . . | 768 | 78 |
| 1982 . . . . . . . . . . . . | 1,274 | 129 |
| *Immoblllzed* **enzymes:** | | |
| 1978 . . . . . . . . . . . . | 25 | $ 1 |
| 1979 . . . . . . . . . !. . | 33 | 2 |
| 1980 . . . . . . . . . . . . | 26 | 2 |
| 1981 . . . . . . . . . . . . | 27 | 2 |
| 1982 .., . . . . . . . . . | 25 | 2 |

a~ata are **probably not COm Plete.**

SOURCE: U.S. Department of Health and Human Services, National Institutes of Health, Office of Recombinant DNA Activities, 1983.

Funding figures for biotechnology research in NIH intramural programs are unavailable; however, this research is a much smaller portion of all NIH-sponsored research.

## National Science Foundation

The total fiscal year 1984 budget request for NSF is $1.2 million, a 17.4-percent increase over fiscal year 1983. Research instrumentation and support for graduate students are high priorities. Within NSF’s Biological, Behavioral, and Social Sci-

“ New projects are those Competing for first time; competing projects are those that are competing but have been funded before by NIH (a competitive renewal); and noncompeting projects are ongoing projects awarded for more than 1 year.

ences program, the physiology, cellular, and molecular biology program is increased 20 percent over fiscal year 1983. The Chemical and Process Engineering Division budget in NSF's Engineering program is also up 21.5 percent; this may have some effect on biotechnology (4).

The total NSF expenditure for grants having some rDNA component from 1975 through October 1982 was just over $57 million. From fiscal year 1975 through fiscal year 1980, about $35.3 million was spent. Funding for grants having some rDNA component in fisca] year 1981 was $9.8 million and in fiscal year 1982, $12.8 million.

## U.S. Department of Agriculture

The fiscal year 1984 budget proposal calls for USDA's agricultural research programs to get along with essentially the same amount of money in 1984 as in **1983 (19).**

The division of funds among USDA's bureaus—the Agricultural Research Service (ARS), the Cooperative State Research Service (CSRS), and the Forest Service—and the USDA research agenda have been the subject of several reports and studies, The latest, from the White House Office of Science and Technology Policy (5), has caused considerable debate. The findings from that report indicate that research at the land-grant colleges and universities lags far behind current developments in plant biology, that agricultural research funds should be more widely distributed, that much of the research conducted by ARS is duplicative, and that the agriculture system overall is no longer energy- nor resource-efficient. In addition, this and other reports have suggested that the competitive grants program within CSRS funds high-quality basic research within USDA and should be expanded in order to create a critical mass of long-term high-quality research. Hearings on this issue are expected in the next year.

In fiscal year 1984, there will bean increase of $4.6 million for the competitive research grants within CSRS in order to initiate a program in animal science. Some of these grants may include biotechnology research. In fiscal year 1981 (latest year for which data are available), of the $15.8 million total being spent for competitive research grants, approximately $5 million was spent on biotechnology research (17).

The Agriculture Committee on Biotechnology of the National Association of State Universities and Land-Grant Colleges (12) has estimated that during 1981-82, $34.7 million was committed to biotechnological research by State Agricultural Experiment Stations (SAES). (This estimate was derived from a survey of SAES that totaled the number of persons plus full-time equivalents working on biotechnological research. ) The distribution of this total is ***42*** percent State, *45* percent Federal, and 14 percent private funding.

ARS has funded a total of $13.6 million in biotechnology research in fiscal year 1983; $7.2 mi]lion of this was devoted to plant biotechnology and $6.4 million to animal biotechnology (27).

## Department of Energy

DOE has several programs involved in biotechnology research. DOE's Office of Basic Energy Sciences, which funds fundamental research in plant sciences and microbiology (photosynthesis, stress mechanisms of plants and micromganisms, genetic mechanisms, methanogenesis, genetics of anaerobic micro-organisms, and regulatory aspects of metabolic pathways), had a budget of $9.9 million in fiscal year 1983 and will have $11.0 million in fiscal year 1984. work on anaerobic digestion, algal production, and genetic manipulation is funded through DOE's Conservation and Renewable Energy programs (including DOE's Solar Energy Research Institute); the budget for these programs is ***$23.7*** million. Other programs support biotechnology research relating to pollutant control, beneficiation of coal, and microbial enhanced oil recovery. The aggregate of these latter activities totaled between $1.5 million and $2.0 million in fiscal year 1983 (14).

## Department of Defense

The Federal agency with the greatest increase in the fiscal year 1984 budget proposal for R&D funding is DOD—up 29.7 percent over fiscal year 1983 in current dollars. Although most of this increase will fall in the development areas of research, a 9-percent increase in basic research is also proposed (18). Within this framework, there are some data available on biotechnology R&D.

The total funding for rDNA basic research over all three military services for fiscal year 1983 is $3.3 million; $2.9 million of this is funded with $0.4 million obligated but not yet funded (2). DOD is currently amassing data on fiscal year 1983 funding for biotechnology- activities (research on cell culture, monoclonal antibodies, etc.). DOD estimates that in-house research is probably at a level of $1 million per year and that contract research in biotechnology is at least as great as that. More accurate figures should be available in fiscal year 1984 (2). These figures represent a very small proportion of the total military basic research budget ($787.5 million for basic research in fiscal year 1983) (19).

## U.S. Government funding of generic applied research in biotechnology

NSF, DOE, DOD, and NIH are the only U.S. Government agencies funding generic applied research in bioprocess engineering. Because of limited Federal support, bioprocess engineering could prove to be a critical bottleneck in the United States as biotechnology moves toward production scale-up. Not only is bioprocess engineering research underfunded relative to other types of engineering research, but trained bioprocess engineers are in short supply. *

The major U.S. Government funding group for generic applied research in bioprocess engineering is NSF's Chemical and Process Engineering Division. In fiscal year 1983, $1.7 million of its $4.5 million budget was used to fund projects in bioprocess engineering. In fiscal year 1984, there is no increase in its budget, but more of the budget, $2.7 million, is being allocated to bioprocess engineering (25).

DOE has a Biocatalysis Research Activity within its Energy Conversion and Utilization Technologies Program. Although this activity was funded up to $525,000 through fiscal year 1983, the administration's fiscal year 1984 budget request implies that biocatalysis research activities will be terminated. This research project, begun in 1981 at $130,000 was a generic applied research project designed specifically to capitalize on basic research conducted at universities. Its goal was to build the technical and engineering base of biocatalysis technology to enable U.S. industry to displace a significant level of nonrenewable resource requirements by the year 2000. The project supported applied research and exploratory development to help establish the technology base that the chemical process industry will need to develop cost-competitive products from genetically manipulated organisms based on renewable energy feedstocks. Unfortunately, this beginning toward a federally funded generic applied research base in bioprocess engineering has been terminated. Currently, however, discussions are underway in DOE's Office of Energy Research to begin a broader bioengineering initiative.

DOD's Defense Advanced Research Projects Agency (DARPA), with an overall budget for fiscal year 1983 of $719.5 million (projected to increase 9.7 percent in fiscal year 1984), has two program areas in biotechnology, one underway and one beginning in fiscal year 1984. Thie first program, a research effort in chemical and biological ultrasensors, began in fiscal year 1982 with a budget of $888,000. Funding for this program is expected to increase to $2.2 million in fiscal year 1983, stay level at about $2,2 million in fiscal year 1984, and increase to $2.9 million in fiscal year 1985. The research is being done through contracts with four universities, two private companies, and three Federal laboratories. The purpose of the second initiative, which is to begin in fiscal year 1984, is to study the mechanical properties of bio-

*See ***Chapter 14: Personnel Availability and Training*** for a discussion of the shortage of bioprocess engineers.

polymers. Funding in fiscal year 1984 will be $1.4 million, rising to $2 million in fiscal year 1985 and 1986, $2.7 million in fiscal year 1987, and decreasing to $1 million for phaseout in fiscal year 1988.

Projects are undertaken in DARPA if there is a perception that there will be downstream applications of interest to the military. Thus, the research DARPA funds is generic applied. If a particular initiative appears to be fruitful, additional funding will he targeted to basic research in the area. Programs are viewed as successful if the technology is transferred to secondary agencies within 5 years. Thus, most research initiatives are for 5 years, at which time they are phased out. New initiatives are continually being phased in as projects demonstrate merit (20).

Although most NIH research is basic research, NIH research on immobilized enzymes, which totaled about $2 million in 1982, could be characterized as generic applied.

# U.S. Government funding of applied research in biotechnology

U.S. Government funding of applied research in biotechnology is provided principally through the Small Business Innovation Research (SBIR) program, a program that was established to promote research by small businesses because only about 1 to 2 percent of the total research budgets of Federal funding agencies were set aside for research by small businesses. The Small Business Innovation Development Act establishing this program was passed in 1982, so it is too early to evaluate it. Furthermore, each Federal agency is implementing the program slightly differently. In several of the agencies, however, there is potential for some funding of applied biotechnology research. The status of the SBIR program with regard to biotechnology in specific Federal agencies is detailed below. Also discussed is the Small Business Set Aside program.

## *Small Business Innovation Research program*

The findings of both Government and private studies on technological innovation in small firms convinced the U.S. Congress of the need to increase the share of Federal R&D dollars going to small businesses. The new Federal SBIR program was created to meet this objective, The SBIR program provides a source of nonequity capital to small businesses in the United States. The SBIR program is designed as an expanded version of continuing smaller programs in DOD and NSF. When the program is fully phased in, nearly $430 million annually will be set aside for small high-technology firms, including many new biotechnology firms (NBFs). *

On July 22, the Small Business Innovation Development Act of 1982 was signed into law by President Reagan. The purposes of this act are to: 1) stimulate technological innovation from Government-funded R&D, 2) use small businesses to meet Federal R&D needs, and 3) increase private sector innovation derived from Federal R&D by coupling the SBIR to venture capital. In the first NSF SBIR solicitation, NSF awards totaled $5.3 million. Approximately $42 million in follow-on funding was awarded to the first recipients.

In order to accomplish the three objectives of the law, the SBIR program is structured in three phases. Phase I is a screening phase to evaluate the technical and commercial feasibility of proposals. Usually, the period of performance is months. The awards given in phase I are up to $50,000. This money is most effectively used for either out-of-pocket expenses and the salary of a technician or for financial sustenance while developing a business plan and looking for venture capital. Only winners of Phase I awards can compete for Phase II awards, and only about so

*NBFs, as defined in ***Chapter 4: Firms Commercializing Biotechnology***, are small firms that have been started-up in recent years specifically to capitalize on new biotechnology.

percent of the Phase I winners receive Phase II awards.

Phase II provides funds for the projects found most promising after Phase I. These awards are generally used for the principal research effort. The period of performance is up to 2 years and the awards given are up to $500,000. In Phase II, the law requests (but does not require) the proposer to obtain a follow-on funding commitment from a third party, usually a large corporation or a venture capital firm. The third party is used not only because the small firms tend to be undercapitalized but also to provide an objective look at the management, market, technology, and long-term financial requirements.

Phase III consists of private investments to stimulate commercial production. This phase is not funded by the Federal Government.

The SBIR law requires that each Federal agency for the next 6 years set aside a specific percentage of its R&D budget for awards to small businesses. Federal agencies with external R&D budgets exceeding $100 million-i.e., the National Aeronautics and Space Administration (NASA), the Department of Health and Human Services (of which NIH is a part), NSF, DOE, USDA, the Department of Transportation, the Department of the Interior, the Environmental Protection Agency, and the Nuclear Regulatory Commission—must set aside 0.2 percent of their external R&D budget for small businesses in fiscal year 1983, 0.6 percent in 1984, 1 percent in 1985, and 1.25 percent in 1986-88. In those agencies with external R&D budgets exceeding $10 billion (DOD), the set aside begins at 0.1 percent and increases to 1.25 percent in the fifth year. Each agency sets its own guidelines for implementation and its own R&D areas for solicitations.

Because the SBIR law is so new, it is difficult to determine the extent to which it might affect technological innovation and the overall competitiveness of N13Fs. Nevertheless, it is clear that the SBIR program gives the U.S. Federal Government an opportunity to influence technological innovation in the U.S. private sector. If biotechnology research areas are given adequate support by Federal agencies, innovations in biotechnology might very well be fostered.

### U.S. DEPARTMENT OF AGRICULTURE

USDA has reserved almost $550,000 for its SBIR program in fiscal year 1983. There are five project areas. The two most likely to initiate biotechnology proposals are animal production and protection and plant production and protection. Solicitations were sent May 1, 1983. USDA anticipates making 10 to 14 awards.

### DEPARTMENT OF ENERGY

DOE has set aside $5.5 million for the SBIR program for fiscal year 1983. One topic of the 25 in the solicitation schedule deals with bioprocess technology and applied microbiology. of the 1,700 proposals DOE received, 100 were on this topic. Traditionally, DOE's relationships with small businesses have been through subcontracting of funds allocated to the National Laboratories and contractors in universities and elsewhere. The work has usually involved procurement of materials, construction, and fabrication rather than research. The SBIR program will provide DOE with another means of supporting applied research in small R&D firms (14).

### DEPARTMENT OF DEFENSE

For fiscal year 1983, DOD has almost $17 million set aside in its SBIR program. Unlike all other Federal agencies, with the exception of NSF, DOD already relies on the small business sector for R&D contracts. In fiscal year 1981, DOD awarded 7.4 percent ($679 million) of its external budget to small businesses—almost twice the small business share of total Federal R&D. Because DOD does not classify R&D projects by industrial application or research area, the amount awarded to small businesses for biotechnology R&D is unknown. *

Because of the important contribution small firms have made to DOD's R&D effort, the Department designed its own SBIR program in 1981—the Defense Business Advanced Technology (DESAT) program—and has made awards to small businesses through that program as well as through regular procurement channels. In fiscal

● DOD's classification system is as follows: 6.1-Basic Research, 6.2-Exploratory Research, 6.3-Advanced Research, 6.4-Engineering, 6.5-Support, 6.6-Major Systems. These headings are not immediately recognizable as biotechnology.

year 1982, **1,103** proposals were received from the first solicitation under the DESAT program and 100 awards were made. The DESAT program will in all likelihood be replaced by the SBIR program.

All three military services plus DARPA participate in DESAT.

- Air *Force.* The Air Force is not pursuing any biotechnology-related R&D with small business or otherwise.
- Navy. In fiscal Year 1982, the Navy granted 36 awards under the DESAT program; few if any of which were in biotechnology-related areas. Other awards were made to small business, but no agency or service is able to break down biotechnology-related contracts for small businesses only, unless they fall under a specific small business program. Most contract research carried out by the Office of Naval Research and the Naval Research Laboratory in the past has been unsolicited. Of the unsolicited business in the past, 48 percent was done by small business and 50 percent was done by universities.
- ***Army.*** Under the SBIR program, biotechnology and chemical defense "correspond to the U.S. Army's 'New Thrust' program designed to take advantage of U.S. technology unmatched by Soviet capabilities that can provide the leverage technologies needed for the future battlefield" (23). The Army's R&D efforts under the SBIR program will emphasize the application of novel technologies such as rDNA and hybridoma technology in the development of vaccines, antidotes, analgesics, and blood substitutes (mostly for casualties). About 3,000 proposals are expected to be received for this topic aIone.
- ***Defense Advanced Research Projects Agency.*** In fiscal year 1983, DARPA has set aside $750,000 for its SBIR program. It is unlikely that more than one biotechnology-related contract will be awarded under the program this year, because there are 14 research areas to be covered and the average contract price is about $50,000. In fiscal year 1982, about 12 percent of all awards went to small businesses. Most proposals that come into DARPA are unsolicited. Earlier in fiscal year 1983, when the schedule for solicitations was being formulated, biotechnology R&D was given the highest ranking for research areas to be pursued. As the schedule went through the review process, however, the specificity of the proposals was changed and the proposals were broadened. A biotechnology effort will, however, be funded in DARPA, in the area of biopolymers. Some of the contract awards will no doubt go to NBFs.

#### DEPARMENT OF HEALTH AND HUMAN SERVICES

The fiscal year 1983 SBIR budget for the Public Health Service, of which NIH is a part, is $5.6 million. Within NIH, it is difficult to speculate about the amount of R&D money to go to NBFs. NIH uses what it refers to as an omnibus solicitation. This approach is designed to generate new business. NIH has little experience awarding applied research contracts to small for-profit companies. In fiscal year 1981, contracts totaling $40 million went to small businesses, mostly for research support (e.g., building animal cages). In fiscal year 1982, the amount increased to $70 million. However, only since January 1982 has NIH been making awards to other types of profitmaking organizations. Most of the forthcoming NIH research solicitations under the SBIR program are in the field of biotechnology.

#### NATIONAL AERONAUTICS AND SPACE ADMINISTRATION

NASA's fiscal year 1983 SBIR program has a budget of $11 miliion. However, biotechnology as defined in this report does not fall within the mission of NASA and is therefore not a NASA research area.

#### NATIONAL SCIENCE FOUNDATION

NSF's SBIR budget for fiscal year 1983 is $5.5 million, approximately the same as the SBIR budget for the Public Health Service. In fiscal year 1982, NSF did not give any awards in biotechnology, and few good proposals were received by NIH. Congressman Don Fuqua sent a letter to NSF and NIH asking why so few proposals for biotechnology research topics were received (6), The response given was that many of the NBFs had received funding from private sources for their first-round financing needs (6). Such firms were ineligible to receive Phase II funding without having participated in Phase I.

### *Small Business Set Aside program*

The Small Business Set Aside program was created to help small businesses obtain Federal Government contracts and subcontracts by setting aside "suitable" Government purchases or competitive awards to small businesses. The set aside contracts (not grants) reserve an entire procurement or a portion of a procurement for the exclusive bidding of small business concerns. The program was designed to give small businesses equal opportunity to compete for Government contracts and subcontracts. It was not designed specifically with R&D contracts in mind and has had limited significance in stimulating technological innovation in small businesses (22).

## U.S. Government instrumentation initiatives

The obsolescence of analytical instruments is an increasingly severe problem for U.S. universities. As instrumentation becomes more sophisticated, it also becomes more costly; furthermore, obsolescence occurs more rapidly. DOD has estimated that upgrading all qualified laboratories to "world class" status in instrumentation would take an infusion of $1.5 billion to $2 billion. Instrumentation is needed not only to carry out research but also to teach the next generation of researchers and industrial personnel.

Since reduced funding levels have caused universities to cut back purchases of necessary technical equipment, a special fund totaling $150 million over 5 years for the purchase of equipment has been set up in DOD. The purpose of the special DOD fund is to upgrade the equipment of universities. Each of the three military services contributes equally to DOD's special fund, and the Office of Naval Research coordinates its administration. The solicitations sent out by DOD stipulate that the requests are to be for major pieces of equipment that cannot be purchased with other funding. One goal of DOD's fund is to stimulate program projects, i.e., to encourage several researchers to work together. The research they would undertake would necessitate the purchase of equipment costing a minimum of $50,000 (this may be raised to $100,000). The primary criterion for evaluating proposals is the relevance of the proposed research to DOD's interests. The second criterion is the scientific merit of the research to be performed with the equipment. By the closing date of November 30, 1982, 2,478 proposals totaling $645 million had been received. The announcement of 204 awards was made in late April 1983, with awards averaging $148,000. The large response to the DOD initiative is one index of the need for updating instrumentation in universities (15).

For fiscal year 1984, major increases in NSF's R&D equipment and instrumentation initiative are proposed (see table 58). Rather than taking the form of a single dedicated line-item, the funding is distributed among the regular disciplinary elements of the budget. NSF stresses that a few manufacturers of equipment recently have agreed to provide substantial discounts for equipment purchased by NSF grantees. Efforts to broaden participation by manufacturers in this program are continuing.

DOE has a $4 million university equipment initiative in fiscal year 1984 for IJOE contractors who need equipment costing more than that allowed in the DOD instrumentation initiative; these requests can have a minimum of about $100,000 (14).

**Table 58.—NSF R&D Equipment and Instrumentation, Fiscal Year 1984 Request** (obligations **in millions of dollars)**

| | Actual FY 1982 | Estimate FY 1983 | Estimate FY 1984 | Increase (percent) F'f 84182 | FY84183 |
|---|---|---|---|---|---|
| Mathematical and Physical Sciences | $41.7 | $ 56.4 | $ 86.3 | 107.0 0/0 | 53.0 "/0 |
| Engineering | 6.4 | 8.7 | 18.3 | 184,4 | 109.2 |
| Biological, Behavioral, and Social Sciences | 14.3 | 16.2 | 24.6 | 72,0 | 51.9 |
| Astronomical, Atmospheric, Earth and Ocean Sciences | 19.6 | 22.1 | 36.7 | 87.2 | 66.1 |
| U.S. Antarctic Program | 6.0 | 6.6 | 12.1 | 101.7 | 83.3 |
| Scientific, Technological and International Affairs. | 2.1 | 2.3 | 2.3 | 9.5 | 0.0 |
| Total, NSF | $90.1 | $112.3 | $180.2 | 100.00/0 | 60.50/o |

SOURCE American Association for the Advancement of Science, */?&D In the FY 1982 Budget A Pre//rn/nary Ana/ys~s.* Washington D C **March 1983**

# International comparisons

A brief overview of Government research funding in the foreign countries expected to be the major competitors of the United States in biotechnology-Japan, the Federal Republic of Germany, the United Kingdom, Switzerland, and France—is presented below.

## *Government funding of biotechnology research in other countries*

The amounts spent by foreign governments on biotechnology research (including basic, generic applied, and applied) are extremely difficult to estimate. Any estimate is at best a guess, and, except where indicated, breakdowns by basic or generic applied cannot be made. Currently available estimates for the countries identified as the major competitors of the United States in the area of biotechnology are as follows:

- ***Japan.*** Funding for biotechnology research in Japan is divided among the Ministry of International Trade and Industry (MITI), the Science and Technology Agency, the Ministry of Agriculture, Forestry and Fisheries, and three other Government agencies. This research is a mix of basic, generic applied, and applied. The figures are shown in table 59.
- ***Federal Republic of Germany.*** Estimates of spending for projects funded by the Federal Ministry for Research and Technology (BMFT, Bundesministerium fur Forschung and Technologies) range from $49 million to $70 million (DM120 million to DM170 million). A large proportion of this research is generic applied.
- ***United Kingdom.*** The British Government is spending about $43.8 million to $52.5 million (<25 million to <30 million) per year on generic applied and applied research in biotechnology. If basic research is included, the figure probably ranges upward toward $60 million.
- ***France.*** Estimates for Government expenditures for biotechnology range from $35 mil-

**Table 59.—Government Funding for Biotechnology Research in Japan, 1982 and 1983 (in miliions)**

| | 1982 | | 1983 | |
|---|---|---|---|---|
| | Yen | Dollars | Yen | Dollars |
| Ministry of International Trade and Industry | + 2,381 | $9.56 | + 2,503 | $10.04 |
| Science and Technology Agency | 2,172 | 8.72 | 2,338 | 9.40 |
| Ministry of Agriculture, Forestry, and Fisheries | 1,874 | 7.53 | 2,017 | 8.10 |
| Ministry of Education, Ministry of Welfare, and Environmental Protection Agency | 7,557 | 30.35 | 7,906 | 31.75 |
| Total | # 13,984 | $56.16 | + 14,761 | $59.29 |

SOURCE G Saxonhowe, "Biotechnology !n Japan" contract report prepared for the Of f!ce of Technology Assessment, U S Congress, June 1983 lion to $60 million (F230 million to F395 million).

## Organization of basic and applied research in other countries

The organization of basic research in the United States and other countries competing in biotechnology is described in ***Chapter 17: University/Industry Relationships and*** in *Appendix* ***B: Country Summaries. The*** organization of generic applied and applied research efforts in countries likely to compete with the United States in biotechnology is outlined below.

### JAPAN

Because of Japan's continuing interest in bioprocess engineering and because MITI has identified biotechnology as a "next-generation" project, there is a great deal of activity in biotechnology research in Japan, Much of the research is carried out by MITI's Agency for Industrial Science and Technology. Some biotechnology projects that MITI is sponsoring are listed in table 60. This agency oversees several research institutes, including the Fermentation Research Institute (FRI). FRI was founded in 1940 to develop fermentation technology and has expanded to include any microbial application in industry and environmental protection. Additionally, FRI has a depository for patented micro-organisms. Its fiscal year 1982 budget was $4.4 million ( 1.1 billion), FRI and other institutes in Japan meet many of industry's needs for generic applied research in biotechnology. Their equivalent does not exist in the United States (16). *

### FEDERAL REPUBLIC OF GERMANY

The Society for Biotechnological Research (GBF, Gesellschaft fur Biotechnologische Forschung) is without doubt the most important of the federally owned research centers for biotechnology in West Germany and perhaps the most ambitious governmentally operated institution of its kind in the world. In 1982, GBF's operating expenses were $13.1 million (DM32 million). Generously funded by the West German Government, GBF is one of the best equipped facilities of its kind in Europe. Its bioprocess laboratory, for example, permits considerable experimentation with bioprocess technology as well as scale-up of biotechnological processes to the pilot-plant stage.

GBF was set up to perform a variety of substantive research tasks as well as to cooperate with other researchers working in the field of biotechnology. GBF's major functions include the following (9):

- to develop environmentally sound biotechnological processes in order to assure a suf -

*For further details, see *Chapter 17: University/Industry Relationships*

**Table 60.—Some Biotechnology Projects in Japan**

| Title of R&D project | Ministry with jurisdiction | Institutions conducting projects | Project period |
|---|---|---|---|
| Utilization of biomass | Ministry of Agriculture, Forestry, and Fisheries | Business Office, Agriculture, Fishery and Forestry Technology Council<br>National Institute of Agricultural Sciences<br>Forestry Experiment Station<br>National Agricultural Experiment Station<br>National Research Institute of Agriculture<br>University and private research institutes | 1980-90 |
| Enzymatic reactors | MITI | National Chemical Laboratory<br>Agency for Industrial Science and Technology | 1979-83 |
| Industrial enzyme use | MITI | Fermentation Research Institute<br>Agency for Industrial Science and Technology | 1980-84 |
| Physiologically active macromolecules and production processes | MITI | Research Institute for Polymers and Textiles<br>Agency for Industrial Science and Technology | 1978-82 |
| Biochemical pulp technology | MITI | Government Industrial Research Institute, Shikoku<br>Agency for Industrial Science and Technology | 1980-83 |

SOURCE: G Saxonhouse, "Biotechnology in Japan, " contract report prepared for the Office of Technology Assessment, U.S. Congress, June 19S3

ficient supply of chemicals, pharmaceuticals, and foodstuffs;
- to scale-up biotechnological processes from the laboratory to the pilot-plant stage, this being the basis for the development of full-scale industrial processes;
- to make new sources of raw materials available for the manufacturing of natural products by micro-organisms and to make plant and tissue cultures available;
- to make new pharmacologically significant natural products available and to investigate their modes of action;
- to make its scientific facilities available to non-GBF research groups, provided that their projects fit within the R&D program of GBF;
- to support other research groups in the fields of biology, chemistry, and medicine by supplying noncommercial natural products;
- to participate in joint projects, provided they are within the framework of BMFT's Biotechnology Program; and
- to provide advanced interdisciplinary training for scientists, engineers, and technicians.

In keeping with its overall mission, GBF is involved in a number of cooperative arrangements with industry and with academic institutions. GBF's resources and expertise are used by industrial and academic researchers, and GBF relies on other institutions, usually private industry, for services such as toxicological and pharmacological testing of new products. GBF is also engaged in joint activities with academic and international research centers. GBF fosters international scientific exchanges by receiving temporary visitors from other countries. An acknowledged objective of BMFT is to strengthen existing ties between GBF and private industry in order to facilitate technology transfer in the field of biotechnology (9).

Since 1979, the German Collection of Micro-organisms (DSM, Deutsche Sammlung von Mikroorganismen) has been incorporated into GBF. DSM has served since October 1981 as an international depository of patented or patent-related micro-organisms pursuant to the Budapest Treaty. * More generally, DSM'S mission is to collect micro-organisms of scientific and technological significance, to conserve them unchanged, and to make them available for R&D and teaching purposes. The proposed budget for operating DSM in 1982 was $833,000 (DM2 million).

## UNITED KINGDOM

The United Kingdom has several Government-sponsored research centers that are involved in biotechnology development projects (see table 61). Some of the centers are entirely Government owned, whereas others have significant industrial commitments.

*See *Chapter 16: Intellectual Property Law.*

**Table 61.—Government-Sponsored Applied Biotechnology Centers in the United Kingdom**

| Name of center | Funding (in millions) | Source of funds |
|---|---|---|
| Center for Applied Microbiology and Research (CAMR) | 4' 2 ($3.5) | Department of Health and Social Security, sales of products, industry contracts |
| British Technology Group (BTG) | ~'13 ($22.8) | Government |
| Celltech | # 12 ($20) | BTG (44°\o)a<br>Technical Development Capital (14VO)<br>Prudential Assurance (14°/0)<br>Midland Bank (140A)<br>British & Commonwealth Shipping Co. (14°/0) |
| Agricultural Genetics | about ~'40 ($70) | BTG (about one-third), Ultramar, Advent Eurofund |
| Biotechnology Institute and Studies Centre Trust | N.A.[b] | Government through: Polytechnic of Central London, University of College London, University of Kent at Canterbury<br>No committed industries |

%TG recently released 1A percent Of its equity to the Rothschild Biotechnology Investments Group and BoO~S co.
bN,A, = information not available.

SOURCE M Vaquin, "Biotechnology in Great Brltaln, "contract report prepared for the Office of Technology Assessment, US. Congress, December 1982, One Government-sponsored center is the Center for Applied Microbiology and Research (CAMR). As shown in table 61, CAMR is financed in part through the Department of Health and Social Security and in part from sales of products and contract research. Its current operating budget is $3.5 million (&'2 million), and there are plans for expansion. CAMR has been singled out by the British Government to play a special role in the development of biotechnology. It has well-developed and established contacts with both universities and industry and sees itself as an intermediary between basic university research and production on an industrial scale. CAMR'S major commercial contract in biotechnology is with KabiVitrum (Sweden) to scale-up and develop a process for manufacture of human growth hormone using rDNA bacteria developed for Kabi by the U.S. firm Genentech. CAMR also has contracts with Cadbury Schweppes (U.K.), Unilever (U.K.), Technofirm Development, Ltd. (U.K.), and Celltech (U.K.).

The British Technology Group (BTG) is a public corporation sponsored by the Department of Industry with the aim of supporting the development of biotechnology by facilitating the transfer of technology from the laboratory to the marketplace (see fig. 31). BTG has committed about $22.8 million (1'13 million) for biotechnology projects to date, with annual increases of $6.5 million projected. BTG has four major investment areas: research support, joint venture funding, startup financing of small firms, and equity and loan financing. It is not clear what portion, if any, of BTG's funds is being used for scale-up and development processes, In addition to and separate from BTG activities, the Department of Industry has initiated a 3-year $30 million "Biotechnology in Industry" program.

Celltech was founded in 1980 by the National Enterprise Board (now BTG), Technical Development Capital, Prudential Assurance, Midland Bank, and British and Commonwealth Shipping Co., with an initial outlay of $20 million (1' 12). Recently, the BTG and Technical Development Capital released 14 percent of their equity to the Rothschild Biotechnology Investments Group and Boots Co. The establishment of Celltech represented one of the first steps initiated by the British Government to involve industry in commercializing the results of research in public sector laboratories. While the company was being formed, it successfully negotiated exclusive access to all work in the Medical Research Council, where monoclinal antibodies (MAbs) were dis. covered in 1975. Although the firm, which intends to concentrate on the development of MAbs for human diagnostic and therapeutic applications, has yet to make a profit on its limited product sales, it has extensive plans for the future, including the development of a continuous cell culture bioreactor that would produce MAbs in higher volumes than current bioprocessing technologies permit.

Agricultural Genetics is a company similar in design to Celltech that will commercialize research of the Agricultural Research Council. BTG will provide about one-third of the capital ($8.6 million; -L'5 million). The industry sponsors are Ultramar and Advent Eurofund.

The Biotechnology Institute and Studies Centre Trust (BISCT) is a recently established organization that draws on the expertise of some of United Kingdom's foremost biotechnologists. Currently, BISCT is offering continuing education in the form of a l-year postgraduate degree in biotechnology, short courses, and an advisory service for industry. It hopes to undertake research programs sponsored by industry in bioprocess engineering and applied microbiology (26).

### SWITZERLAND

Switzerland has no publicly owned research institute specifically for biotechnology comparable to GBF in West Germany. outside industry, research related to biotechnology, both basic and applied, is carried out primarily in the university system, which at present includes 10 institutions of higher learning.

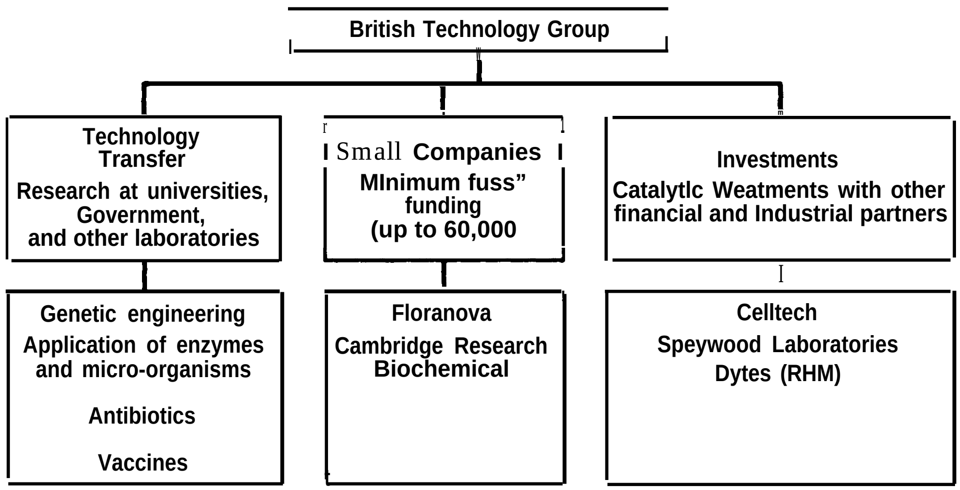
The leading Swiss center for research on the generic applied and applied aspects of biotechnology is at the Federal Institute of Technology (ETH, Eidgenossiche Technische Hoschschule) in Zurich, one of the two polytechnic universities managed by the Federal Government through the Swiss School Council (Schweizerischer Schulrat). Headed by a former research director of the Swiss pharmaceutical company Hoffmann-La

**Figure 31 .—British Technology Group Support for Biotechnology**

BTG Support for Biotechnology

Support research
- Joint venture funding
- . Minimum-fuss finance for small firms
- Equity and loan finance

Total funds committed by BTG: f13 million




Biotechnology Subject Areas Being Supported

| | |
|---|---|
| Agricultural applications | 8 projects |
| Industrial applications | 8 projects |
| Medicinal applications | 17 projects |
| Veterinary applications | 4 projects |
| Enabling technology | 2 projects |

Strategy for Further Investment

Seek out and promote:

- Opportunities for industrial investment in downstream applications of genetic engineering and cell fusion
  — Low volume, high margin products
  — Healthcare, food production and fine chemicals

Respond positively to:

c Technology transfer opportunities from universities and public sector laboratories
  — Back a lot of starters
  — Involve potential industrial partners as early as possible

s Opportunities for industrial investments in “biotechnology infrastructure”:
  — Laboratory reagents and equipment
  — Fermentation hardware

Avoid:

c Early investment in “big biotechnology” projects
  — e.g., heavy organic chemicals, bioenergy, and waste recovery

SOURCE Brltlsh Technology Group, Prutec Ltd., and Technical Development Capital, “Minutes of Evidence to Education, Science, and Arts Committee on Biotechnology,” H. M, Stationery Office 289iil, April 26, 1982

Roche, ETH proved receptive to the idea of biotechnology at a fairly early date, and its department of biotechnology was established in 1976. One of the department's achievements to date is the development of a new bioreactor design, which is being tested along with more conventional models in the ETH bioprocessing facility.

The channels for transfer of knowledge from the universities to industry appear well established in the area of biotechnology, although the large pharmaceutical companies may not yet be major beneficiaries of this exchange. The president of ETH, for example, has endorsed the practice of industrial contracts with professors in the biotechnology department. Joint funding by industry and the Commission for the Encouragement of Scientific Research provides another avenue for collaboration with the private sector, one that has been actively utilized by the ETH biotechnology group. The Swiss firm Biogen S.A. * is not only closely linked to the Swiss university research system, but has built an important share of its competitive strength on the productivity of these ties (8).

## FRANCE

France has no Government-sponsored applied research centers like GBF in West Germany and the ETH-Zurich in Switzerland. The Institut Pasteur, a nonprofit organization jointly sponsored by the Government and industry, is the single most important facility in biotechnological research in France, but is primarily concerned with basic research. The Institut Pasteur receives 47 percent of its income from the French Government (Directorate General for Research). The rest of its income comes from the sale of services: royalties from Institut Pasteur Production (13 percent), industrial contracts (33 percent), and donations collected by the Association for the Development of Institut Pasteur (7 percent). Although the Institut Pasteur is mostly concerned with basic research (e.g., projects on vaccines and monoclinal antibodies), it does support the development aspects of biotechnology (e.g., projects on the use of cellulose for alcohol production and biological insecticides) with industrial contracts.

The Institut Pasteur has plans to open a new biotechnology building in 1985 or 1986. This building, which will have 3,000 square meters of new laboratory space, will be used partly to rehouse existing projects and partly for new projects. It will also contain bioprocess scale-up facilities (at present, the Institut Pasteur cannot do any scale-up work itself). The new biotechnology building is to be financed by the Government, but the Institut Pasteur will have to cover the operating costs, probably by increased industrial contracts,

An organization within the Institut Pasteur, G3, was started several years ago to encourage applied research in rDNA technology. G3 is funded by a set of Government groups: Institut Pasteur, the National Center for Scientific Research (CNRS, Centre National de la Recherche Scientifique), the National Institute for Agricultural Research (Institut National de la Recherche Agronomique), and the National Institute of Health and Medical Research (INSERM, Institut National de la Sant6 et de la Recherche M6dicale). G3 has no capital, cannot employ directly, and does not own any laboratory space. It only has an operating budget. Now working with a staff of only 10, G3 plans to expand into the new biotechnology building. The work program is proposed in part by the Government partners and in part undertaken at the request of industries. It is too early to predict whether G3 will contribute significantly to a generic applied research program in bioprocess technology (25).

● Biogen N.V., the parent company of the Biogen group, is registered in the Netherlands Antilles, Biogen S.A., one of Biogen N.V.'s four principal operating subsidiaries, is located in Switzerland, along with Biogen N.V.'s principal executive offices.

# Findings

U.S. Government expenditures for basic research in biotechnology-the largest in the world —amount to approximately $511 million per year (mix of data from fiscal years 1982 and 1983). U.S. Government expenditures for generic applied research in bioprocess engineering and applied microbiology are estimated to be approximately $6.4 million (see table 56), although the amount could possibly range as high as $20 million or $30 million if the portions of USDA and DOE expenditures devoted to generic applied biotechnology research were known. U.S. Government funded applied research in biotechnology is virtually nonexistent, except for the SBIR program and some work being done in the National Laboratories. Most of NIH's solicitations for the SBIR program and about 5 percent of DOE's are for biotechnology; if all solicitations are funded, this could total about $5 million plus. The U.S. Army has also included a major initiative for biotechnology under its SBIR program. Since none of these grants has been funded, it is too early to estimate the amounts that will be devoted to applied biotechnology research.

Data on Government expenditures on biotechnology research in Japan are the best for purposes of international comparisons. The total amount being spent by the Japanese Government for biotechnology research in Japan is about $60 million, but Japan's definition of biotechnology is a broad one. A significant proportion of the Japanese Government's funding is for generic applied research in bioprocess engineering. The Federal Republic of Germany, United Kingdom, and France are probably spending similar amounts for biotechnology research (approximately $60 million to $100 million each), probably with relatively equal portions of basic and generic applied research.

The current pattern of U.S. Government funding for basic and generic applied research in biotechnology in the United States may compromise the U.S. competitive position in the commercialization of biotechnology. There is no doubt that past Federal support for basic research has produced a scientific infrastructure and knowledge base in the United States that is the best in the world. Furthermore, continued Federal support of basic research is critical for future innovation in a high-technology society. Because the U.S. Government has provided comparatively little funding for generic applied research, however, Americans may not be as efficient as the Japanese in applying the scientific base to the development of marketable goods and services. The Japanese Government's funding for generic applied research allows companies in Japan to make optimal use of the basic scientific knowledge of the United States and other countries and very efficiently develop this knowledge into marketable products. U.S. industry draws on the basic science knowledge base also, but the speed of the diffusion and development of this knowledge may be slower and ultimately more costly than it would be if more generic applied research were funded by the U.S. Government.

In comparison with other types of engineering research, as well as with molecular biology research, bioprocess engineering research in the U.S. is severely underfunded by the Federal Government. The personnel and academic research needs are enormous. If current funding levels for bioprocess engineering research are not increased, the United States' competitive position in biotechnology may not be as strong in the future as it is now. Bioprocessing expertise currently rests in private industry (chiefly in the pharmaceutical industry). Because private industry's bioprocessing research is proprietary, the diffusion of generic applied knowledge in this area is not as rapid as it might be. Industrialists generally agree that roughly 20 person-years of engineering research are required to go from the test-tube stage to the point where the design of a plant can begin. (Each person-year costs from $80,000 to $120,000). If existing processes or engineering techniques can be used, then about 8 instead of 20 person-years of engineering research are required. The 12 person-year difference is partially attributable to generic applied research that is now duplicated among companies at great cost. Generic applied research in bioprocess engineering could, at least partially, be supported by Federal funds. Federal support could ensure more rapid diffusion of generic applied knowledge, thus enhancing U.S. competitiveness in biotechnology.

In Japanese universities, there is a clear separation between basic and generic applied research. In addition, the Japanese Government supports generic applied research through institutes such as FRI. Japan currently is increasing its funds to basic research, although it relies to some extent on the basic research of the United States.

GBF, generously funded by the West German Government, is one of the best equipped applied biotechnology research centers in Europe. Its bioprocess laboratory, for example, is excellent. In its various activities, GBF also serves as a bridge between academia and industry.

The United Kingdom has a high standard of excellence and a cadre of highly trained basic research personnel. Recently, the British Government funded either wholly or in part several institutes and organizations to carry out generic applied and applied research and to train researchers in industry in the new techniques. These include CAMR, a center to carry out generic applied microbiology research and diffuse it to industry; Celltech, a company formed to exploit public sector microbiology research; Agricultural Genetics, a company formed to exploit public sector agricultural research; and BISCT, a biotechnology institute and studies center trust to offer continuing education, especially to industrialists.

Switzerland has an excellent basic research base in molecular biology, especially considering its small size. In addition, ETH in Zurich undertakes applied research and in 1976 established a biotechnology department. ETH and faculty at universities have a tradition of close interaction with industry in Switzerland.

In France, universities are regarded as teaching rather than research institutions. The Government funds its own laboratories through CNRS or INSERM. These laboratories are attached to several universities. The most important center for biotechnology research is the Institut Pasteur which is funded jointly by the Government and industry and carries out primarily basic research. G3, an organization established several years ago within the Institut Pasteur, was specifically mandated to encourage applied research in rDNA technology. It is too early to predict whether G3 will contribute significantly to the development of the field. The major lack in French biotechnology is a supply of trained researchers, because the biological disciplines have not traditionally been favored in France.

Basic, generic applied, and applied research are necessary for any country's competitive position in biotechnology. In terms of funding of basic research, the United States is clearly the leader with the largest and most extensive basic research enterprise in the world. The United Kingdom, West Germany, and Switzerland follow, and Japan is slightly behind them. France is sixth because it only now is beginning to exert a concerted effort to study molecular biology.

In contrast, the Japanese Government leads all countries in its commitment to generic applied and applied research. The West German Government also has an extensive commitment to generic applied research with the best equipped generic applied research laboratory in Europe. The United Kingdom and Switzerland follow. The United Kingdom is beginning to fund applied efforts with its support, for instance, of Celltech and Agricultural Genetics, and Switzerland, with ETH, has had a biotechnology effort since 1976. The United States ranks behind these four countries in its relative commitment to generic applied research as opposed to basic research, and is followed by France, which ranks sixth in all three categories of research.

# Issues and options

**ISSUE 1: How could Congress improve U.S. competitiveness in biotechnology by promoting generic applied research?**

With its continua] support of basic research, Congress has endorsed a Federal commitment to long-term funding of basic research that is essential to technological development and innovation in this country. It is crucial to the U.S. competitive position in biotechnology that this commitment to basic research continue.

Over the last three decades, the Federal commitment to generic applied research in biology and Bioprocess engineering has declined relative to the commitment to basic research. Researchers in the United States have not been attracted to fields such as applied microbiology or bioprocess engineering because only small amounts of Federal funding have been available. Two critical factors underlie this decline: 1) there is no flexible, broad-based Federal system for carrying out such work; and 2) there has been a steady erosion of these generic applied science efforts in U.S. universities.

The governments of the major industrial countries of Western Europe and Japan all possess generally effective and sometimes extensive mechanisms for funding generic applied R&D. Furthermore, the university systems of these countries have not become as unaware of the needs of industrial technology as have the universities in the United States (7). To improve U.S. competitiveness in biotechnology by promoting generic applied research, Congress could adopt one or more of the following options. *

***Option 1: Fund one or more biotechnology institutes within universities.***

The interdisciplinary nature of biotechnology requires interaction among people with backgrounds in biology and engineering, but most American universities are not structured to facilitate this interaction. The creation at selected campuses of biotechnology institutes, in which faculty in both biology and engineering could be located in the same physical structure and work on common research projects, could facilitate this interaction. These institutes could carry out basic and generic applied research. Funding could come from Federal and State Governments and from industrial sources. Several States have already begun development of biotechnology centers; Federal funding might help leverage State funding to bring in more industrial support. Industrialists as well as academicians could work in the institutes; this arrangement would foster domestic technology transfer. In addition, students could be trained in both academic and industrial environments and industry personnel could be retrained at the institutes.

***Option z: Increase funding for university -industry cooperative programs within NSF.***

NSF currently has two university/industry cooperative programs. One, the Industry/University Cooperative Research Projects program, encourages industry/university cooperation for basic research because it will fund up to half of the cost of a grant for basic research projects involving the cooperation of investigators from industry and universities. The program is advantageous to industry, because it allows industry to leverage its research funding effort, and, through cooperation, to gain a competitive edge in the innovation process. University researchers benefit from the program as well, because they improve their awareness of industrial problems and applications of basic research work.

The other NSF program, the Industry/University Cooperative Centers program, provides seed money for a university to set up a center in cooperation with industrial partners. Federal funding is phased out after 3 to 5 years. This program allows the establishment of settings that encourage university/industry cooperative research, while market demand helps to determine the type of research to be undertaken. Government funding adds incentive for industry to fund long-term, generic applied research. The infrastructure for

* S(IIJ *Chapter 12 Financing and Tax Incentives for Firms* for indirect funding options for R&D.

the continued implementation of the program already exists within NSF.

The peer review system for reviewing university/industry cooperative research projects at NSF is separate from the system for reviewing other research projects. Thus, the generic applied nature of these cooperative research projects is taken into consideration, while high standards of research are assured.

Although increased Federal funding for university/industry cooperative programs within NSF could promote generic applied research, if the funding is not supplemental to needed increases in basic research in bioprocess engineering, the cooperative program could be damaging to the extension of fundamental knowledge in bioprocess engineering and applied microbiology.

***Option 3: Establish special grants for interdepartmental cooperative research in biotechnology.***

Currently, there is little communication between bioprocess or chemical engineers and basic biologists in universities. Special grants stipulating that a bioprocess engineer and a biologist be coprinciple investigators on a cooperative research project could make researchers in these disciplines more likely to conduct research on bioengineering or applied microbiology research relevant the commercial development of biotechnology. The grants could be administered by NSF, since it has the technical personnel to administer such a program.

One potential problem with special grants, given current difficulties in obtaining funding, is that the researchers might cooperate in order to write the proposal then do essentially separate pieces of research once funding is obtained. Thus, the research conducted might not be truly cooperative. Avoiding this problem would necessitate carefully stated requests for proposals and careful monitoring of research.

***Option 4: Develop generic applied research capability for biotechnology in the National Laboratories.***

The National Laboratories are an existing resource, both in terms of physical plant and personnel, that would be expensive to duplicate. Currently, the National Laboratories do not have a great deal of expertise in biotechnology, Nevertheless, there would be several advantages to developing their generic applied research capability. These laboratories have a commitment to research, facilities to conduct research, an objective attitude towards industrial development, an array of personnel trained in relevant disciplines, and unique instrumentation development capabilities that could have a major impact on biotechnology development. DOE's Energy Research Advisory Board has just assessed the laboratories, and the White House Office of Science and Technology Policy is currently reviewing them. An assessment of the capability of the National Laboratory system to carry out generic applied research in biotechnology has not been a part of this report. This is an option for further study by Congress.

***Option 5: Increase funding for the SBIR program.***

Increased funding for the SBIR program would foster applied research not only in biotechnology but also in other high-technology areas. Furthermore, this program maintains the traditional philosophy of keeping much of applied research in industry and fostering entrepreneurship.

Two counterarguments to this option should be mentioned. First, although DOD and NSF have had programs similar to the SBIR program, the SBIR program has not been in existence long enough in other agencies to be evaluated. Second, because SBIR-funded research must have commercial potential within 3 years, it is too short term for problems that are generic applied, i.e., studies that fall between fundamental research and applied research. The SBIR program, as it is structured, is funding research that is further on the continuum toward product development than generic applied research. Although the program is important for biotechnology because it could help support small businesses that are doing biotechnological research, it may not be a viable option for increasing support of generic applied research in biotechnology.

### ISSUE 2: Should the U.S. Government fund a germplasm screening program?

USDA (under ARS) has a network of centers for accession, storage, screening, and research on germplasm. The work at most of the centers is devoted to study of plants (the center at Fort Collins, Colo., being the largest). The center in Peoria, Ill., however, also includes micro-organisms in its collection. The Peoria center currently houses about 80,000 accessions of micro-organisms (pathogens are not included in the program) of potential interest to bioprocesses, especially for foods and drugs. It also houses 15,000 accessions of wild plant species and is screening these for industrial and medical potential. Of these, 8,000 wild species have been analyzed. Since the Peoria center is a repository for patented and industrially important micro-organisms, there is no specific program to screen these or other micro-organisms for potentially useful genes. The National Academy of Sciences is currently reviewing the USDA germplasm storage program in order to evaluate the relative efforts spent on accession and storage versus screening and analysis for potentially useful genes. A germplasm screening program might be an oversight issue for Congress as biotechnology develops.

### ISSUE 3: How could Congress help U.S. academic institutions meet their needs for modern equipment and instrumentation?

There is an enormous need for modern equipment and instrumentation at universities, colleges, and secondary schools. Instrumentation is needed for teaching as well as research purposes, because teaching and research institutions have not been able to meet the needs for rapidly changing technology in instrumentation. In addition, as research grows more sophisticated and specialized, the instrumentation also grows more costly. To enable academic institutions to meet their needs for equipment and instrumentation, Congress could adopt one or more of the following options.

*Option 1: Increase the special DOD fund for upgrading university equipment.*

The purpose of DOD's fund, obligated in fiscal year 1982 and totaling $150 million over 5 years, is to upgrade university equipment. The solicitations stipulated that the equipment must be for basic research, must be multiuser, and must cost more than $50,000. By the closing date, proposals totaling $645 million had been received from U.S. universities. An increase in funding would help to alleviate the huge need manifested by the $645 million in proposals.

One disadvantage of relying exclusively on the instrumentation fund in DOD is that DOD awards are granted only to projects that are of interest to DOD. A second problem is that DOD's fund does not address equipment needs in the $10,000 to $50,000 range.

*Option 2: Increase the instrumentation fund within NSF.*

The NSF research instrumentation initiative is slated for major increases in fiscal year 1984, with the biological sciences component up 51.9 percent and engineering up 109 percent (some portion of which will be spent on bioprocess engineering). The NSF funds will concentrate on multiuser equipment. Various manufacturers of equipment have agreed to give NSF grantees reduced prices for purchase of this equipment.

The NSF research instrumentation initiative, although it moves in the right direction toward reducing instrumentation needs, is a part of the awards process. That is, more money will be available only for NSF grantees to use for instrumentation needs for NSF-funded research projects. Instrumentation initiatives similar in amount to DOD's but without the defense-related restrictions do not exist in the United States. An instrumentation initiative within NSF or some other agency could be steadily increased over the next several years to begin addressing the instrumentation needs of teaching and research institutions. Some funds could be earmarked for instrumentation needs primarily for teaching purposes.

*Option 3: Legislate tax deductions for the installation and servicing of new or used equipment that companies have donated to universities*

Tax deductions to encourage industry to donate equipment to universities and colleges already exist. Often, however, because they cannot afford the installation and service costs, universities are unable to use the equipment that is donated. A change in the tax law to stipulate that installation charges and even service maintenance charges would also be tax deductible would increase the university research benefit of the measure.

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