Chapter 2

Introduction and Overview

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INTRODUCTION

For more than four decades, American political tradition has called for strong Federal support of basic research. In contrast, Federal support and policies related to applied research have been inconsistent—more related to changing national security needs, and more reflective of global economic competitiveness and differing political views. While the debates over Federal support of basic research were essentially settled in the affirmative in the late 1940s, debate over technological development and application has continued over the years, often technology by technology. In recent years, a new dimension has been added to the debates, stimulated by the belief that the United States has suffered some loss of international economic competitiveness due to the relative decline in its scientific and technological capabilities.

This new dimension is reflected in keen interest in and a focus on questions related to the Federal Government's roles and policies in supporting, affecting, and facilitating the levels and patterns of industrial innovation. Much of this interest arises from the belief that the ability of the United States to improve and maintain its present standard of living depends on its ability to maintain and enhance its competitive position in the provision of goods and services derived from application of advanced industrial technologies. Debates on these issues in the context of various high technologies, such as biotechnology, are likely to continue in the times immediately ahead due to concerns about the trade deficit and U.S. industrial competitiveness.

Far more than an opportunity for economic predominance in biotechnology is at stake. **The wide-reaching potential applications of biotechnology lie close to the center of many of the world's major problems-malnutrition, disease, energy availability and cost, and pollution.** Biotechnology can change both the way we live and the industrial community of the 21st century because of its potential to produce:

- products never before available,
- products that are currently in short supply,
- products that cost substantially less than products made by existing methods of production,
- products that may be safer than those now available, and
- products made with raw materials that may be more plentiful and less expensive than those now used (4).

Policymakers are interested in biotechnology because of its potential for improving health, food production, and environmental quality, and because it is seen as a strategic industry with great potential for heightening U.S. international economic competitiveness. These expectations logically lead to questions of whether current levels of funding are adequate and properly focused and whether the United States should use additional methods to promote research and development in this diverse area. As in other areas of science and technology, there are fundamental questions about the obligations and roles of various institutions in promoting and regulating these technologies. Traditionally, basic research has been supported by the Federal Government, applied research and development has been the domain of industry, and the States have invested in both, depending upon the needs of their economies.

The ubiquitous nature of biotechnology makes it the focus of several areas of public policy. Biotechnology relies on the expertise of a multitude of collaborative scientific and engineering disciplines in both the basic and applied sciences, requiring support across a wide range of fields. The multidisciplinary nature of biotechnology has extensive implications for governmental, educational, and industrial structures, suggesting diverse incentives for action. The allocation of resources to build the necessary scientific and technological base and to provide for the regulation and control of resulting products, processes, and uses is a fundamental role of government.

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The tools of biotechnology allow manipulation of biological organisms in ways that will greatly increase their utility, thereby motivating industrial applications. Furthermore, the Nation's educational institutions are affected by biotechnology because of its dependence on strong research capabilities, a highly skilled workforce, and its encouragement of intersectoral relationships.

While biotechnology has taken on a "trade" status, with its own firms, newsletters, investment funds, and regulations, it is not a single industry but a set of enabling technologies applicable to a wide range of industries As full integration of biotechniques occurs, each sector of industry developing biotechnology-based products will face different opportunities for and barriers to commercialization. The ability to recognize similarities and differences between sectors will be critical to policymaking as new products are ready for marketing and strategies for promoting and regulating biotechnology products are developed.

Because these advances make significant commercial and social gains possible, government and industry share an interest in promoting biotechnology research and development. This report examines the current level of investment in biotechnology research, development, and training by Federal and State Governments, industry, and collaborative arrangements among sectors. It also describes the nature of the research being funded and identifies scientific and institutional gaps and barriers to developing this new set of technologies. **This report focuses on the positive and negative financial, human, scientific, and institutional inputs into the development of biotechnology.** As the title of the report implies, spending allocated to the development of biotechnology can be considered an investment because of expectations that resources so dedicated will result in future benefits. Much more difficult to assess is whether expenditures are reasonable for future growth and whether expenditures are proportionate to those being made in addressing other national needs. Finally, to understand the reasons for investment in biotechnology, the ultimate products of research and the paths to application are also discussed in three case studies.

The following section discusses the definitional issues surrounding biotechnology and describes the problems associated with accurately assessing U.S. investment in biotechnology.

ASSESSING U.S. INVESTMENT IN BIOTECHNOLOGY: LAYERS OF COMPLEXITY

In preparing this report, OTA estimated levels and directions of U.S. investment in biotechnology by surveying Federal agencies, State agencies, and private industry. In addition, four workshops were held with attendees from Federal, State, and local governments, industry, and academia (see app. C for workshop participants). The first workshop, titled "Public Funding of Biotechnology Research and Training," was held in September 1986 (10). Representatives of Federal and State agencies presented budget data for biotechnology and discussed the implications of the varying definitions of terms. OTA obtained updated budget information in fall 1987.

In April 1987, representatives from academia and industry met at OTA to discuss "Collaborative Research Arrangements in Biotechnology" (3). In June 1987, biotechnology industrialists were convened to discuss "Factors Affecting Commercialization and Innovation in the Biotechnology Industry" (5). Finally, in July 1987, a workshop was held to discuss "Public and Private Sector Roles in Funding Agricultural Biotechnology Research" (11).

The OTA surveys, workshops, and informal communications with representatives of all sectors interested in biotechnology revealed two methodological dilemmas in assessing U.S. investment in biotechnology: variation in the definition used to describe biotechnology and variation in the methods used to account for biotechnology investment. Each of these difficulties is discussed below.

Defining Biotechnology

In a 1984 report, after extensive canvassing of academicians, industrialists, and government officials involved in biotechnology, OTA arrived at two definitions of biotechnology. The first definition is broad, encompassing both old and new biotechnology, and includes any technique that uses living organisms (or parts of organisms) to make or modify products, to improve plants or animals, or to develop micro-organisms for specific uses. Since the dawn of civilization, people have deliberately selected organisms that improved agriculture, animal husbandry, or brewing. **To differentiate between biotechnology using more traditional techniques from the newer techniques developed in recent years, OTA uses a second, more narrow definition of biotechnology. This definition refers only to "new" biotechnology: the industrial use of recombinant DNA, cell fusion, and novel bioprocessing techniques (4). As in the earlier report, the term biotechnology, unless otherwise specified, is used here in reference to new biotechnology.**

Photo credit: Amgen

Preparation of a DNA sequencing gel to analyze structure of a gene for porcine somatotropin.

The current study focuses on R&D investment in fields affected by new biotechnologies. Three main areas of research relevant to biotechnology:) can be described: basic, generic applied, and applied (4). Basic research involves biotechnology by using its component tools (e.g., recombinant DNA and hybridomas) to study the different ways in which biological systems work and to identify the mechanisms that govern how they work. Included in this category are studies that address such questions as how viruses infect cells, how immunity to pathogens is acquired, and how fertilized egg cells develop into highly complex and specialized organisms. Biotechnology is used in a broad range of scientific disciplines, ranging from microbiology (the study of micro-organisms such as viruses and bacteria) to biophysics (the use of physical and chemical theories to study biological processes at the molecular level). A greater understanding of the mechanisms of evolution and the resilience of ecosystems will also come from new biotechnology.

The phrase "generic applied research" is thought by some to be vague and ambiguous; however, it is useful for describing research that bridges the gap between basic science done mostly in universities and the applied, proprietary science done in industry for the development of specific products. Various groups have coined alternative phrases, such as '(bridge" research, "technical" research, and "strategic" research. Examples of generic applied biotechnology research are the development of general methods for protein engineering and large-scale mammalian or plant cell culturing.

Applied research is directed toward a very specific goal. The use of recombinant DNA to develop vaccines for specific antigens, such as malaria or the HIV virus responsible for Acquired Immunodeficiency Syndrome (AIDS); the transfer of herbicide or pesticide resistance to a particular plant species; and the use of monoclinal antibodies as purification tools in bioprocessing are all examples of biotechnology use in applied research.

In the current political environment, where promotion of high technology is strongly favored, the definitions used for biotechnology have important ramifications. The terms used to describe biotechnology can affect research funding and the regulatory treatment of potential commercial products. Some groups believe that any confusion about what biotechnology is could be alleviated by substituting more specific terms such as gene therapy, protein engineering, and bioprocess engineering, for the general term "biotechnology" (1).

A recent General Accounting Office (GAO) report, titled '(Biotechnology: Analysis of Federally Funded Research" (2), used three categories to calculate levels of biotechnology funding at five Federal agencies. They are:

1. Basic research in the sciences underlying biotechnology.
2. Applied research and technology development using the new techniques of biological research. This work is done to devise, apply, or improve products and processes.
3 Research pertinent to the regulation of biotechnology products and processes.

It is the second category–applied research—that presents the most confusion in determining the extent of public and private investment in biotechnology.

Since the definition of biotechnology varies among funding sources, figures presented without explanation could create myths that would become difficult to dispel. Therefore, instead of requesting each Federal agency to report funding levels only as they pertain to a uniform definition of biotechnology, OTA asked each to offer its own definition of biotechnology (see ch. 3). For the surveys of industry investment in biotechnology, the respondents were requested to account for research related to biotechnology in general and to each of three specific categories of new biotechnology: recombinant DNA techniques; cell fusion technology; and novel bioprocessing methods.

Accounting for Investment in Biotechnology: The Pitfalls

Accounting for U.S. investment in biotechnology is a formidable task. As described above, the definitional dispute adds to the complexity of a process that must also recognize sectoral differences in accounting and reporting. In addition,

Photo credit: Cetus

Industrial scientist successfully clones and expresses the *E. coli* methionine aminopeptidase enzyme.

within each sector—Federal, State, and private—there may be as many differences as there are parties. Within the Federal Government, OTA collected budget data from 11 different executive agencies, each with its own system of accounting for budgets and expenditures. In a survey conducted by OTA, 33 States reported a variety of mechanisms for determining their level of investment in biotechnology. In addition, OTA surveyed small, dedicated biotechnology companies and larger, diversified and established corporations with significant investments in biotechnology, to determine levels of investment, areas of application, number and type of employees, and factors affecting commercialization. Although certain accounting procedures are standardized in industry, those used in reporting R&D can be vague and strategically motivated. Pitfalls specific to the assessment of investment in biotechnology in each sector are summarized below.

Assessing Federal Investment

Aggregate estimates of total Federal support for biotechnology are still rough and preliminary.

There is no easy or systematic way by which Federal agencies can separately account for dollars being dedicated to biotechnology. Because the tools developed from biotechnology have been fully integrated into both basic and applied work in so many areas of research, separating out "biotechnology-related work" is an arduous task with suspect results. Biotechnology draws from established fields such as biology, chemistry, and engineering, and is seldom identified separately in an agency's budget. In addition to differences in mechanisms of accounting for specific research expenditures, agencies vary in their definition of biotechnology, making estimates of total Federal spending speculative, and cross-agency comparisons difficult to interpret.

Assessing State Investment

At the State level, few budgets list research appropriations in general, let alone biotechnology, as a line item in their budget. Research and development funds are derived from several lines in a budget and are directed to several recipients. Thus, undercounting or overcounting can easily occur, depending on the perspective or biases of the accountant. In addition, operating budgets for biotechnology initiatives may be derived from several sources other than State coffers, such as Federal research agencies and philanthropic organizations. States facing this dilemma provided OTA with estimates of investment. Furthermore, as with Federal reporting, the definition of biotechnology used by the reporting States affected how funds were accounted and programs initiated.

Assessing Private Investment

Two problems were faced in evaluating investment by the private sector. First, the identification of firms investing in biotechnology is problematic. Some firms call themselves biotechnology companies when, in fact, they do not fall within the OTA definition. Other, more traditional companies may be conducting important research in biotechnology but do not consider themselves a biotechnology firm, and do not identify themselves as such. Large corporations may be multinational, with several subsidiaries, making identification of programs and budgets complex.

Second, even when a reliable list of firms is available, gathering information from the identified companies is difficult. Firms that are privately held—as defined by the Securities and Exchange Commission-often do not divulge relevant financial information, resulting in inevitable undercounting of dollars devoted to biotechnology. In addition, some forms of investment by public firms, such as research contracts or licensing agreements, need not be divulged, compounding the problem. Thus, any accounting of total private investment in biotechnology is likely to be an underestimate.

ORGANIZATION OF THE REPORT

This report is organized to present U.S. biotechnology investment data in several ways. Chapters 3, 4, and 5 present analyses of investment in biotechnology by the Federal Government, the States, and industry, respectively. Resources dedicated to biotechnology and the implications of the distribution and use of those resources are discussed. Chapter 6 summarizes factors affecting innovation and commercialization of biotechnology. Chapter 7 presents an analysis of university-industry collaboration in biotechnology as an important device used to facilitate research and development. Chapter 8 presents the results of an OTA survey of U.S. training programs in biotechnology and discusses personnel needs in industries commercializing biotechnology.

Chapters 9, 10, and 11 assimilate many of the issues presented in the first eight chapters into a specific industrial framework. Because it is difficult to draw conclusions across all industries regarding the influence of any one factor on biotechnology, OTA analyzed three industries in particular. Chapter 9 discusses U.S. investment in biotechniques applied to human therapeutics. The application of biotechnology to human therapeutics is the first and greatest growth area of applied biotechnology and has matured to the point where more traditional concerns, such as patenting and regulation, are influencing application as much as funding levels. Chapter 10 examines investment in biotechnology applied to plant agriculture and issues that affect the dollar flow into R&D in that field. Plant agriculture is considered to be the next growth area of biotechnology. Finally, the application of biotechnology to hazardous waste management, as the least technically advanced application of biotechnology of the three fields examined, is discussed in chapter 11.

SUMMARY

This report is a comprehensive survey of investment in biotechnology within the United States. **The levels of U.S. investment in biotechnology presented in this report are informed estimates.** The reader is best served, however, by looking beyond the numbers and recognizing the enormity and diversity of efforts underway within the United States to support research in biotechnology and to promote its application. **Because of the uncertainties in the estimates, reliance on the numbers alone obscures the full picture.**

Numerous issues, other than the level and type of resources invested, direct and affect biotechnology research and development. These factors include the structure of research relationships, quality and availability of personnel, effects of regulations and controls, intellectual property law, and export and trade policy. While many of those issues are discussed within the context of this report, the reader is referred to other reports in the series New **Developments in Biotechnology.** They are *Ownership of Human Tissues and Cells (7), Public Perceptions of Biotechnology (9), Field Testing of Engineered Organisms: Genetic and Ecological Issues (6),* and *Patenting Life (8).*

CHAPTER 2 REFERENCES

1 Miller, H .1., and Young, F. E., "Biotechnology: A 'Scientific' Term in Name Only, " *The Wall Street Journal,* Jan. 13, 1987.

.2. U.S. Congress, General Accounting Office, *Biotechnology: Analysis 01" Federal@ Funded Research,* RCED-86-187 (Washington, DC: September 1986).

3. U.S. Congress, Office of Technology Assessment, "Collaborative Research Arrangements in Biotechnology, " transcript of workshop proceedings, Apr. 23, 1987.

4. U.S. Congress, Office of Technology Assessment, *Commercial Biotechnology: An International Analysis,* OTA-BA-218 (New York, NY: Pergamon Press, Inc., January 1984).

5. U.S. Congress, Office of Technology Assessment, "Factors Affecting Commercialization and Innovation in the Biotechnology Industry, " transcript of workshop proceedings, June 11, 1987.

6. U.S. Congress, Office of Technology Assessment, *New Developments in Biotechnology: Field Testing of Engineered Organisms: Genetic and Ecological Issues, OTA-BA-350* (Washington, DC: U.S. Government Printing Office, May 1988).

7. U.S. Congress, Office of Technology Assessment, *New Developments in Biotechnology: Ownership of Human Tissues and Cells, OTA-BA-337* (Washington, DC: U.S. Government Printing Office, March 1987).

8. U.S. Congress, Office of Technology Assessment, *New Developments in Biotechnology: Patenting Life,* forthcoming, fall 1988.

9. U.S. Congress, Office of Technology Assessment, *New Developments in Biotechnology." Public Perceptions of Biotechnology,* OTA-BP-BA-45 (Washington, DC: U.S. Government Printing Office, May 1987),

10. U.S. Congress, Office of Technology Assessment, "Public Funding of Biotechnology Research and Training, " transcript of workshop proceedings, Sept. 9, 1986.

11 U.S. Congress, Office of Technology Assessment, "Public and Private Sector Roles in Funding Agricultural Biotechnology Research, " transcript of workshop proceedings, July 23, 1987.