Chapter 2

Introduction

"The United States is the world leader in biotechnology. This $2 billion domestic industry is expected to increase to $50 billion by the year 2000."

Vice President Dan Quayle
The President's Council on Competitiveness
Report on National Biotechnology Policy

"It is industries, not nations, that compete globally."

Gail D. Fosler
Chief Economist, The Conference Board

CONTENTS

Box

Figure

Tables

INTRODUCTION

This report examines international trends in biotechnology-related commercial activity and governmental approaches to promotion and regulation of biotechnology. This introductory chapter provides a context for the report's more technical chapters by explaining and defining what biotechnology is, by outlining some factors that influence competitiveness in biotechnology, and by describing the congressional request for this report and the organization of the Office of Technology Assessment's (OTA's) assessment of issues raised by the requesters of this report.

WHAT IS BIOTECHNOLOGY?

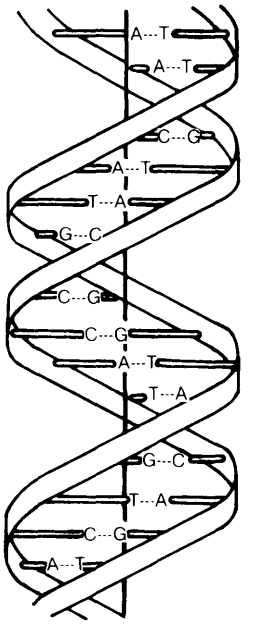
The first challenge in describing the effect of biotechnology on a global economy is to define biotechnology. The term "biotechnology" means different things to different people. Some view biotechnology as all forms of biological research. To others, biotechnology includes the use of classical breeding techniques that have been used for years to create new plants, animals (e.g., improved livestock), and foods (e.g., baking and brewing). Others view biotechnology as comprising modern biological techniques (e.g., rDNA, hybridoma technology, or monoclinal antibodies) that have resulted in greatly increased understanding of the genetic and molecular basis of life (see figure 2-l). Some people have analogized biotechnology to a set of new tools in the biologist's toolbox, by referring to "biotechnologies. To Wall Street financiers and venture capitalists who invested in the creation of companies in this area, biotechnology represents a hot, new source of financial risk and opportunity. Congress, increasingly involved in public policy questions raised by biotechnology, in one statute referred to products "primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site-specific genetic manipulation techniques' (35 U.S.C. 156(2)(B)).

In a 1984 report, after extensive canvassing of academicians, industrialists, and government officials involved in biotechnology, OTA arrived at two definitions of biotechnology (3). The first definition—broad in scope-described biotechnology as 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. This definition encompasses both new biological tools as well as traditional uses of selecting organisms for improving agriculture, animal husbandry, or brewing. A second, more narrow definition refers only to "new" biotechnology: the industrial use of rDNA, cell fusion, and novel bioprocessing techniques. It is the development and uses of this new biotechnology that has captured the imagination of scientists, financiers, policymakers, journalists, and the public. As in earlier OTA reports, the term "biotechnology," unless otherwise specified, is used in reference to new biotechnology.

COMMERCIALIZATION OF BIOTECHNOLOGY

Biotechnology-both as a scientific art and commercial entity—is less than 20 years old (see table 2-l). Science, however, can find roots in the

Figure 2-l—The Structure of DNA



SOURCE: Office of Technology Assessment, 1991.

Table 2-l—Major Events in the Commercialization of Biotechnology

1973	First cloning of a gene.
1974	Recombinant DNA (rDNA) experiments first discussed in a public forum (Gordon Conference).
1975	U.S. guidelines for rDNA research outlined (Asilomar Conference). First hybridoma created.
1976	First firm to exploit rDNA technology founded in the United States (Genentech). Genetic Manipulation Advisory Group started in the United Kingdom.
1980	Diamond v. Chakrabarty--U.S. Supreme Court rules that micro-organisms can be patented. Cohen/Boyer patent issued on the technique for the construction of rDNA. United Kingdom targets biotechnology for research and development (Spinks' report). Federal Republic of Germany targets biotechnology for R&D (Leistungsplan). Initial public offering by Genentech sets Wall Street record for fastest price per share increase ($35 to $89 in 20 minutes).
1981	First monoclinal antibody diagnostic kits approved for use in the United States. First automated gene synthesizer marketed. Japan targets biotechnology (Ministry of International Trade and Technology declares 1981, 'The Year of Biotechnology"). Initial public offering by Cetus sets Wall Street record for the largest amount of money raised in an initial public offering ($1 15 million). Over 80 new biotechnology firms formed by the end of the year.
1982	First rDNA animal vaccine (for colibacillosis) approved for use in Europe. First rDNA pharmaceutioal product (human insulin) approved for use in the United States and the United Kingdom.
1983	First expression of a plant gene in a plant of a different species. New biotechnology firms raise $500 million in U.S. public markets.
1984	California Assembly passes resolution establishing the creation of a task force on biotechnology. Two years later, a guide clarifying the regulatory procedures for biotechnology is published.
1985	Advanced Genetic Sciences, Inc. receives first experimental use permit issued by EPA for small-scale environmental release of a genetically altered organism (strains P. syringae and P. fluorescens from which the gene for ice-nucleation protein had been deleted.
1986	Coordinated Framework for the Regulation of Biotechnology published by Office of Science and Technology Policy. Technology Transfer Act of 1986 provides expanded rights for companies to commercialize government-sponsored research.
1987	U.S. Patent and Trademark Office announces that nonhuman animals are patentable subject matter. October 19th-Dow Jones Industrial Average plunged a record 508 points. Initial public offerings in biotechnology-based companies virtually cease for 2 years.
1988	NIH establishes program to map the human genome. First U.S. patent on an animal-transgenic mouse engineered to contain cancer genes.
1989	Bioremediation gains attention, as microbe-enhanced fertilizers are used to battle *Exxon Valdez oil* spill. Court in Federal Republic of Germany stops construction of a test plant for producing genetically engineered human insulin. Gen-Probe is first U.S. biotechnology company to be purchased by a Japanese company (Chugai Pharmaceuticals).
1990	FDA approves recombinant renin, an enzyme used to produce cheese; first bioengineered food additive to be approved in the United States Federal Republic of Germany enacts Gene Law to govern use of biotechnology. Hoffman-LaRoche (Basel, Switzerland) announces intent to purchase a majority interest in Genentech. Mycogen becomes first company to begin large-scale testing of genetically engineered biopesticide, following EPA approval. First approval of human gene therapy clinical trial.
1991	Biotechnology companies sell $17.7 billion in new stock, the highest 5-month total in history. Chiron Corp. acquires Cetus Corp. for $660 million in the largest merger yet between two biotechnology companies. EPA approves the first genetically engineered biopesticide for sale in the United States.

SOURCE: Office of Technology Assessment, 1991.

discovery of the replication process of deoxyribonucleic acid (DNA)--first proposed nearly 40 years ago by Francis H.C. Crick and James D. Watson (1,10,1 1)—and commerce in standard fermentation techniques, which is centuries old.

The commercialization of biotechnology, both in terms of research and the development of products and services, has received increased attention during the 1980s. The promotion of high-technology is of increasing concern—both in terms of alleviating social problems such as hunger, disease, and pollution—and in terms of creating new sources of wealth for national economies. In a short period of time, biotechnology has joined a menu of other high-technology fields, viewed as being important to the future development of the U.S. economy.

Three main areas of research relevant to biotechnology can be described (see box 2-A). Biotechnology provides the potential to produce new, improved, safer, and less expensive products and processes. Pharmaceuticals and diagnostics for humans and animals, seeds, whole plants, fertilizers, food additives, industrial enzymes, and oil-eating microbes are just a few of the things that can be created or enhanced through biotechnology.

It is convenient to refer to biotechnology as though it were a singular, coherent entity, and in some respects, commercial activity in biotechnology is unique. Federal spending for biotechnology-related research can be estimated, and the linking of such activities under the term "biotechnology' is seen by many as useful for obtaining adequate research and development (R&D) funding. At least 33 States are actively engaged in some form of promotion of biotechnology R&D. Such efforts are seen as a means to achieve academic excellence in their colleges and universities, as a path to economic development, or both. In U.S. industry, OTA has identified more than 400 dedicated biotechnology companies (DBCs) and 70 established corporations with significant investments in biotechnology (8). Many of these companies, especially the DBCs, share common political concerns (as represented by the formation of various biotechnology organizations) and business traits (e.g., methods of financing or means of product development). On Wall Street, biotechnology is recognized in some business reports as a portfolio of stocks—in much the same manner as other technologies and industrial sectors are so recognized.

Box 2-A—Three Kinds of Research

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 biotechnology.

Generic applied research is a useful term for describing research that bridges the gap between basic science, done mostly in universities, and 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 include----the development of general methods for protein engineering and large-scale mammalian or plant cdl-culturing.

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

SOURCE: Office of Technology Assessment, 1991.

Because biotechnology has become an essential tool for many existing industries, there is no such entity as the biotechnology industry. Rather, biotechnology is employed by several industrial sectors, each with its own advantages and obstacles in the race to market (see table 2-2). As DBCs develop products and services, these companies are facing many of the opportunities and obstacles faced by the industrial sector in which they seek to compete.

Table 2-2-Some Factors That Can Affect Commercialization of Biotechnology

Antitrust law
Applied research
Basic research
Collaborative ventures
Congressional interest
Coordination between agencies
Cost of capital
Environmental control
Equipment
Export controls
Gaps in knowledge
Government targeting policies
Industrial capability
Intellectual property protection
Joint ventures
Legislation
Marketing agreements
Mergers
Personnel availability
Public and private funding
Public opinion
Regulations
Statutes
Tax incentives
Technology licensing
Technology transfer
Trade
Undergraduate and graduate education
University/industry relationships

SOURCE: Office of Technology Assessment, 1991.

Table 2-3-Requesters of OTA Assessment, *Biotechnology in a Global Economy*

Senate
Committee on Agriculture, Nutrition, and Forestry
Committee on the Budget
Committee on Governmental Affairs
House
Committee on Science, Space, and Technology

SOURCE: Office of Technology Assessment, 1991.

As commercial biotechnology expands in size and scope, its effect on the international economy is likely to increase. Biotechnology is likely to be seen as a national asset by more nations—both as a way to develop a high-technology base and to increase market share in several international industrial sectors. As the use of biotechnology expands, various factors and barriers come into play. Some of these factors are business-specific, some industry-wide-specific, and some recognizable across the range of industries affected by biotechnology.

ORGANIZATION OF THE REPORT

The report, which was requested by several congressional committees (see table 2-3), has two parts. The first part, ***Commercial Activity, examines*** some of the ways biotechnology has influenced the following sectors: financing, health, agriculture and food, chemicals, and environmental applications. The second part, ***Industrial Policy, examines the*** role of government in forming policies concerning science and technology, regulations, and intellectual property. Appendixes focus on a summary of biotechnology in 14 countries, U.S. Federal Government funding of biotechnology R&D, and a comparison of biotechnology in the United States and Japan.

Because biotechnology is so ubiquitous and its applications so far-reaching, it is impossible to study in depth all the ways it may be used and all the ways it may affect the economies of various nations. Instead, this report focuses on general trends in each area and uses case studies, as appropriate, to highlight relevant economic and policy considerations.

This report is the latest in a series of OTA reports on the subject of biotechnology. Earlier reports addressed: ***Impacts of Applied Genetics (2), Commercial Biotechnology (3), New Developments in Biotechnology (4,5,7,8,9),*** and ***Mapping of the Human Genome (6).*** This report does not focus on specific issues addressed in earlier OTA reports, but rather, draws on them to examine some of the emerging issues related to the globalization of biotechnology. Its primary focus is on the description and analysis of commercial activity in biotechnology-related services and products—in both industrialized and newly industrializing nations. Issues solely related to biotechnology development in Third World nations is beyond the scope of this report.

Three public meetings were conducted by OTA in order to develop information for this report. A workshop of Federal agency representatives was held in May 1989. A 2-day international conference was held in July 1989 that brought together representatives from 16 nations. A workshop on financing issues was held in September 1990 (see app. D for the participants of these meetings). The proceedings of the international conference as well as other selected contract documents are available through the National Technical Information Service (see app. F).

SUMMARY

Biotechnology, broadly defined, 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 purposes. Although traditional uses of biotechnology are centuries old (e.g., baking and brewing), it is the so-called new biotechnology involving the uses of modern scientific techniques, such as rDNA technology, hybridoma technology, and bioprocess technology, that leads to issues affecting international commercialization of research and products and is the focus of this report.

Biotechnology is not an industry. It is, instead, a set of biological techniques developed through decades of basic research that is now being applied to research and product development in several existing industrial sectors. The arrival of biotechnology has resulted in the development of products and processes that have the potential to alleviate many of mankind's problems, e.g., malnutrition, disease, and pollution. This report examines international trends in biotechnology-related commercial activity and industrial *policy.*

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