



Introduction

Biotechnology, an industry built on fundamental breakthroughs in the understanding of genetic processes, is barely three decades old. Biotech is widely perceived to be the next great frontier of scientific advancement that will bring with it whole new industries. The potential economic impacts of new technologies, though unknown, seem to be huge.

Clearly, the competition to be a biotech center will be keen. Who will triumph? For those metropolitan areas that do not already have a strong biotechnology industry cluster, what will it take to develop one?

The relevance of biotechnology breakthroughs to people's daily lives has become increasingly clear. In June 2000 an international team of researchers announced that they had completed mapping the human genome, an accomplishment compared to Isaac Newton's physics observations. This biotech advancement is predicted to lead to a new era of medicine in which scientists develop treatments and vaccines that target the molecular underpinnings of disease. In recent months, attacks using Anthrax spores have heightened public awareness of the potential of bioterrorism and have also triggered demand for the antibiotic Cipro.

The interest in biotechnology is especially strong among those involved in promoting economic development. A survey of 77 local and 36 state economic development agencies reported that 83 percent have listed biotechnology as one of their top two targets for industrial development (Grudkova 2001). Some 41 states have undertaken programs or activities to stimulate the development of biotechnology (Battelle Memorial Institute, State Science and Technology Institute, *et al.* 2001). Clearly, the competition to be a biotech center will be keen. Who will triumph? For those metropolitan areas that do not already have a strong biotechnology industry cluster, what will it take to develop one?

The present survey examines the location and intensity of biotechnology activity in the 51 U.S. metropolitan areas with populations of a million or more. It offers a systematic assessment of various measures of biomedical research and biotech commercialization, the two primary components of a strong and successful industry. There exists no single universally agreed-upon definition of biotechnology, but the range of data sources presented in the survey offers a variety of complementary perspectives on the varying facets of the biotechnology industry. The analysis is based on the composite picture provided by these various data sources.

The unit of analysis is the census-defined Metropolitan Statistical Area (MSA), with the Bureau of the Census list used for ranking metropolitan areas by population. Census combines adjacent metropolitan areas having strong commuting ties into consolidated metropolitan statistical areas; the report follows that same convention in grouping and ranking metropolitan areas. For brevity, these metropolitan areas are referred to by the name of the principal or largest city (or in some cases, cities) in the metropolitan area, even though all of the data are tabulated for the entire metropolitan area. Our sample includes the 51 metropolitan areas in the continental United States and San Juan -Caguas-Arecibo, in the Commonwealth of Puerto Rico.

Overview of the Biotechnology Industry

Biotechnology is the application of biological knowledge and techniques pertaining to molecular, cellular, and genetic processes to develop products and services. The biotechnology industry, as it defines itself, consists of firms established to develop this knowledge and to exploit it commercially. Biotechnology has potential applications in a wide variety of industries. It is already used in agriculture (genetic engineering of plants and animals for food and fiber), in manufacturing (food processing and chemical engineering), and even in computing (bio-computers)—all of them important although often related more closely to nonmedical uses of biotechnology. The largest category of biotechnology applications is in health and medicine: diagnosing, treating, and in some cases preventing disease. Standard and Poors estimates that human diagnostics and therapeutics account for 95 percent of biotechnology revenues (Standard and Poors 2000). Because diagnostics and therapeutics constitute the largest segment of the biotech industry, the report focuses on these applications of biotechnology. (A fuller description of the report's industry definition is contained in the appendix.)

Biotechnology is not synonymous with medical technology or even with high-tech medicine. Many medical technologies and disciplines are unconnected to genetic and cellular manipulation. A wide variety of medical-device manufacturers produce everything from diagnostic instruments to surgical tools to physical prostheses, but these producers are considered to be largely outside of the area of biotechnology, as are firms developing software or information technology for medical records, epidemiology, and other such purposes. These are all important technologies, but they are generally unconnected to the genetic and cellular

techniques that are the hallmark of biotechnology. (An important exception is the production of software and tools for gene sequencing and analysis.)

Biotechnology firms are not separately classified as such in either the Standard Industrial Classification System or in its successor, the North American Industry Classification System (NAICS). Instead, most biotechnology firms are assigned to one of two broader industry categories encompassing research and development and drug manufacturing—namely, NAICS five-digit industry 54171 (Research and Development in the Physical, Engineering, and Life Sciences) or NAICS industry group 3254 (Pharmaceutical and Medicine Manufacturing). For the purposes of gathering statistical data, the present report focuses on these two classifications.

Structure of the Pharmaceutical and Biotechnology Industries

The pharmaceutical industry and the biotechnology industry have a number of important characteristics that distinguish them from each other and from other industries. There follows a brief overview of the history and development of these two industrial sectors, their current structures, and some of the important aspects of the regulatory and competitive environment surrounding firms in each one of them.

The 1997 Economic Census provides data on the number of firms, employment, and sales by firms in the pharmaceutical and life science industries (**table 1**). (As noted earlier, these industry categories include a broader set of activities than simply biotechnology.) In 1997 the pharmaceutical and biotechnology industries represented by these industry classifications had total sales of nearly \$105 billion and employed about 300,000 persons in the United States. The industry has added about 100,000 jobs in the last 15 years, although year-to-year employment

growth has been uneven, declining in the mid-1990s but rebounding and growing rapidly in the final years of the decade.

The industry classifications shown in **table 1** comprise many different types of firms, including pharmaceutical manufacturers and makers of a wide variety of related products including vitamins, herbs, blood derivatives, anesthetics, antiseptics, and medical mouthwashes. The bulk of employment and sales is accounted for by large vertically integrated pharmaceutical manufacturers. No separate category exists for biotechnology firms, which are defined not by their products but by the technologies they use. Biotechnology firms are generally defined as those firms founded for the purpose of applying biological knowledge and techniques to develop products and services. The present survey adopts the common definition of biotechnology used by firms in the industry, by the industry’s leading trade association, and by investment analysts and adopted by the majority of comprehensive academic studies of the industry.

Biotechnology research firms tend to be small and fairly recently established and to devote most of their resources to research and development. Pharmaceutical firms are much larger and much

older and have well-developed manufacturing and marketing operations, often worldwide in scale. The world’s pharmaceutical industry is led by U.S.–based giants like Merck and Bristol-Myers-Squibb and by European-based firms like Bayer and Novartis. **Tables 2 and 3** provide a list of the ten top-grossing biotech and pharmaceutical firms in the United States.

Firms tend not to move between these two categories—small biotech firms, even extraordinarily successful ones, do not grow into large pharmaceutical firms. Instead, biotech research firms tend to sell or license their technologies to larger pharmaceutical firms, or to form joint ventures with them, or to sell them their entire companies. The different business skills required and the high cost of scaling up to global-scale manufacturing and distribution usually discourage small research firms from growing internally.

The result is huge differences in the apparent optimal scale of biotech research firms and that of pharmaceutical firms, appropriately referred to as “Davids” and “Goliaths.” The typical pharmaceutical corporation is four decades older than the typical biotech research firm and a hundred times larger (measured by employment or sales) (Dibner 1999). For instance, according



TABLE 1: PHARMACEUTICAL AND BIOTECHNOLOGY INDUSTRY EMPLOYMENT AND SALES (UNITED STATES, 1997)

NAICS	Industry	Companies	Employment	Sales (in \$ thousands)
325411	Medicinals/Botanicals	312	23,378	11,920,571
325412	Pharmaceuticals	710	115,781	67,520,044
325413	Diagnostic Substances	202	36,502	8,145,884
325414	Biological Products, except Diagnostic	268	23,285	5,685,943
5417102	Research and Development in the Life Sciences	4,044	98,279	11,722,721
Total		5,536	297,225	104,995,163

Source: Census Bureau, 1997 Economic Census.

TABLE 2: SALES RANK OF TEN LARGEST U.S. BIOTECH COMPANIES, 1999

Rank	Biotech Company	Headquarters	Sales (\$)
1	Amgen Inc.	Los Angeles	3,340,100,000
2	Biogen Inc.	Boston	794,435,000
3	Genzyme Corp	Boston, MA	772,288,000
4	Immunex Corp	Seattle	541,718,000
5	Life Technologies Inc.	Basel, Switzerland	409,609,000
6	Medimmune Inc.	Washington, D.C.	383,375,000
7	Nabi	Boca Raton	233,603,000
8	Charles River Laboratories Inc.	Boston	219,276,000
9	Gilead Sciences Inc.	San Francisco	168,979,000
10	Serologicals Corp	Atlanta	129,744,000
Total			6,993,127,000

Source: PriceWaterhouseCoopers Edgarscan (2001).

TABLE 3: SALES RANK OF TEN LARGEST U.S. PHARMACEUTICAL COMPANIES, 1999

Rank	Pharmaceutical Company	Headquarters	Sales (\$)
1	Merck & Co., Inc..	New York City	32,714,000,000
2	Bristol-Myers-Squibb Co.	New York City	20,222,000,000
3	Columbia Laboratories Inc.	Miami	18,921,074,000
4	Pfizer Inc.	New York City	16,204,000,000
5	American Home Products Corp.	New York City	13,550,176,000
6	Abbott Laboratories	Chicago	13,177,625,000
7	Warner Lambert Co.	New York City	12,928,900,000
8	Eli Lilly & Co.	Indianapolis	10,002,900,000
9	Schering Plough Corp.	New York City	9,176,000,000
10	Pharmacia & Upjohn Inc.	New York City	7,253,000,000
Total			154,149,675,000

Source: PriceWaterhouseCoopers Edgarscan (2001).

to revenue rankings of publicly traded U.S.-based firms, Amgen, the largest U.S. biotech company, would be smaller than each of the ten largest pharmaceutical firms. The tenth-largest U.S. pharmaceutical firm has sales (\$7.25 billion) in excess of the combined sales of the ten largest biotech firms (\$6.99 billion).

The geography of the pharmaceutical and biotech firms tends to differ as well. The United States has the largest

concentration of biotechnology research firms, but many of the world's largest pharmaceutical firms are located in other nations, particularly in Europe. Global leaders in pharmaceuticals include Novartis (Switzerland), Hoffman-LaRoche (Switzerland), Glaxo-Wellcome (Great Britain), and Bayer (Germany). Not only do these firms sell their products in the United States but also many of them have U.S. subsidiaries or joint ventures with U.S. firms. Six of the nation's ten largest pharmaceutical firms

are headquartered in the New York-Philadelphia corridor, but none of the ten largest biotech firms is found in that area (PriceWaterhouseCoopers Edgarscan data, based on 1999 sales).

There also exists a great difference in profitability between biotechnology firms and pharmaceutical firms. Most small biotech firms are losing money. According to Ernst and Young, the typical biotech firm spent \$8.4 million on research and development and earned revenues of \$2.5 million in 1998. In contrast, pharmaceutical firms tend to be extremely profitable. Merck & Company, one of the largest pharmaceutical houses, had net income of \$4.6 billion that same year, an amount greater than the collective \$3.4 billion loss of all of the biotech research firms combined.

Differences in size are reflected also in differences in industry volatility. Biotechnology firms regularly rise and fall, according to industry observers: Dibner (2000) estimated that half of the biotech firms formed since the 1970s had folded or were merged into other companies. Pharmaceutical firms tend to be much more long-lived, despite the recent wave of mergers among the pharmaceutical industry leaders (which has produced even larger firms).

The pharmaceutical sector and the biotech sector are characterized by very widespread intersectoral ties between firms. These ties take the form of cross-ownership, licensing, joint ventures, and research agreements. Large pharmaceutical firms often invest in promising research at smaller biotech firms. Small firms obtain access to the pharmaceutical firms' regulatory expertise and manufacturing and marketing capability. Firms frequently share technology: Recombinant Capital (2001), a research firm specializing in the biotechnology industry, reports more than 10,000 industry alliances during the 1990s.

Economics of Biotechnology

The distinctive economics of biotechnology greatly shapes the development of the industry. The process of developing new biopharmaceutical products is uncertain, time consuming, and expensive.

Biotechnology is a risky business. Improved understanding of genetics has led to some novel and successful therapies, but relatively few research projects lead directly to new products. In a given year, the National Institutes of Health (NIH) will fund about 25,000 research projects. Researchers and private companies get an average of 5,500 patents for new biotechnology in a given year. Around 400 biotech medicines are in development, but only about 100 biotech-related drugs have reached the market in the past 30 years, with the top ten accounting for nearly all of the sales (Standard and Poors 2000).

The process of developing new biotechnology projects is time consuming. Not only is there considerable work in research before a drug is developed but also any promising products must endure lengthy testing and clinical trials to prove their safety and efficacy. Development of a new drug typically takes between five and twelve years (Dibner 1999).

The high level of uncertainty of success and the great length of time required to develop biotech products make biotech development a costly proposition. Biotech firms need to pay for expensive medical research, laboratory facilities, and legal fees many years in advance of any likely sales revenue and with uncertain prospects of success. This reality makes large amounts of patient, up-front capital an essential ingredient for successful biotechnology firms.

Role of Government Policy

In many respects, biotechnology is the quintessential knowledge-based industry. Genetic material is analogous to encoded information. Many of the advances in biotechnology stem from applying information technology to developing a better understanding of how genetic processes work and what genes are responsible for which traits and diseases.

It is no surprise then that intellectual property is a defining feature of the biotechnology industry. Biotechnology involves the creation of new ideas through research, the development of new products and processes embodying these ideas, the testing of the efficacy of these products, and the communication of this information to physicians and patients.

Government policy plays an important role in almost every stage of the biotechnology industry. Government support for basic and applied research provides much of the knowledge on which new products are based. The government heavily subsidizes the training of medical researchers. Patents on drugs, on diagnostic products, and most recently on gene sequences codify the ownership of particular kinds of knowledge. The country's patent policy is set by Congress and administered by the U.S. Patent and Trademark Office. Most biotechnology products cannot be offered for sale unless their safety and efficacy have been approved by the Food and Drug Administration. The FDA also regulates the conditions for manufacturing pharmaceuticals and for advertising them to consumers. Finally, government policies on health care, particularly the decision of whether to include coverage for particular drugs or therapies in national health care programs like Medicare and Medicaid, influence the demand for drugs.

It is difficult to overstate the importance of these governmental decisions to the performance of this industry. Everything from fundamental questions of policy—can a gene sequence be patented?—to mundane administrative trivia has a profound effect on industry development. For instance, at one point the patent office had accumulated a backlog of more than 11,000 biotechnology-related patent applications, producing enormous uncertainty over property rights and product development (Dibner 1999).

Methods

The study aims to identify the top biotechnology clusters in the United States, using data gathered on various aspects of biomedical research and commercialization in order to ascertain the relative amount of biotechnology activity in 51 metropolitan areas. Biomedical research capacity and activity were examined first, as measured by employment and education, NIH funding levels, and the number of biotechnology patents issued in each metropolitan area. Biotechnology commercialization activity was then assessed by looking at the level of venture capital funding, the value of research contracts with pharmaceutical companies, the level of initial stock market offerings, the number of biotechnology firms with 100 or more employees, the number of new biotechnology firms established during the 1990s, firms' market capitalization, and firms' membership in industry associations.

The composite measures were constructed as follows. For each variable, such as NIH funding, the average level of activity was computed for the 51 metropolitan areas in the sample, and the level of activity in each metropolitan area was indexed to this overall average. For each metropolitan area, a composite measure of activity was then computed as the average of its index scores on each of the variables.