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Policy Brief Number 1

The Biomedicine Industry in California: Overview and Policy Considerations

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1. The Biomedicine Industry

The biomedicine industry is difficult to define. Some observers use "biomedicine" and "biotechnology" (biotech) as interchangeable labels. Others characterize biomedicine more narrowly as a sub-set of biotechnology.[1] In this paper, we distinguish biomedicine from biotech by considering industry segments that focus primarily on human health.[2] These segments have the inherent ability to change completely how medicine is practiced. They range from companies engaged in basic science research that seeks to modify use of biological processes to develop new biopharmaceuticals and therapeutics to companies involved in the design and manufacture of new treatment devices, and those developing new diagnosis and testing technologies

1.1. Origins

Biotech-like innovation became a part of the human experience as early as the Bronze Age when someone discovered how to use yeast to make beer and leaven bread. But biomedicine was not distinguished from academic biology and medicine until three decades ago despite the fact that the components essential to biomedicine such as the microscope and the first understandings of cell structures date from the 17th century. The industry's evolution traces from and is inexorably linked to advances in scientific knowledge and to the "marriage" between science and the marketplace. Economists began noticing the commercialization of science in the mid-19th century. This "transformation of science into capital" remains the quintessential aim of the industry.[3]

Biomedicine as we know it counts the contributions of legions of extraordinarily talented scientists, engineers, physicians, inventors, and tinkerers as well as visionaries and risk-takers in business, finance, and government. It also results from the stability and predictability of our system of laws, including patent law and copyright protection for intellectual property, and by responsiveness of the marketplace to scientific innovation

Success in the marketplace builds on the positive value our culture gives to medicine, the faith we have in the inevitability of medical progress, and the widespread acceptance by the public that medical progress is inherently good. The marketplace for biomedicine works, too, because of the trust Americans generally place in the integrity of the nation's regulatory system. "The expectations of the public are simple but very high: bioscience discoveries will inevitably lead to technological innovations that become incorporated into products and services that continue to enhance the quality of human life. Whether such expectations can continue to be satisfied at such a high level into the future is difficult to predict for certain, but the odds for a modest amount of continued growth of the industry overall seem reasonable."[4]

Although any number of innovations may be antecedents, four benchmarks spaced about 25 years apart frame the industry's growth. Alexander Fleming's culturing of the first antibiotic substance from mold in 1928 ranks as a significant early event. The 1953 discovery by Francis Crick and James Watson of how nucleic acids can pair to form a self-copying code of a DNA molecule is another. A third was the 1973 finding by researchers at UCSF and Stanford University, made possible with funding from the National Institute of Health, of technology to insert foreign, functioning genes into bacteria by recombinant DNA methods. The start-up of Genentech a few years later by the same UCSF scientist, Biochemist Herbert Boyer, and venture capitalist Robert

Swanson, demonstrated the start-up business model pervasive in the industry today. The model depends on venture capital and other forms of private sector investment to build upon intellectual property developed with federal funding at universities and other research entities and transfer it to the marketplace. The fourth benchmark, the 2001 announcement of the success of the Human Genome Project, has kicked off work throughout the world that promises to dramatically change almost all biological and medical research as investigators seek to use human genes, proteins, and antibodies to create new classes of medicines.

1.2. Overview

Biomedicine companies range from the very small, with no earnings and uncertain prospects, to multibillion-dollar earners. Access to capital, always a challenge in business, is especially problematic for fledgling biomedicine companies.

Though sometimes slowing because of generalized slowing in the economy, public and private investment in the industry has nevertheless increased steadily.

> Sometimes people ask me what field I'd be in if not computers. I think I'd be working in biotechnology. I expect to see breathtaking advances in medicine over the next two decades, and biotechnology researchers and companies will be at the center of that progress. Bill Gates[5]

1.2.1. *Growth*

Industry expansion and the continuing worldwide leadership of U.S. biomedicine can be attributed to factors such as:

1. Public and private sector investment in life sciences education (biology, medicine and related disciplines) and laboratory and computer infrastructure at the major research universities;

2. Public and private investment in basic and applied research;

3. Academics and other university-based researchers willing to support the commercial use of their intellectual work;

4. Universities willing to facilitate campus-industry interaction;

5. The clustering of biomedicine companies near the major research universities create a “critical mass” that attracts scientific talent and generates other economies of scale;

6. Discovering stimulated by the fluid and reciprocal movement of talent and ideas between universities and companies;

7. Cultures, on and off campus, supporting entrepreneurship;

8. Federal legislation and regulation enabling commercialization of government supported knowledge work; and,

9. Investors willing to make intensive capital investments and years-long investment in research and development (R&D) processes.

1.2.2. *The Industry Today*

Access to capital is crucial. Companies surviving the critical start-up period may need sustained capital for 10 years or more before they generate sufficient revenues to meet their R&D goals and operational expenses. In the industry today:

- 35 percent of firms are publicly traded,
- 50 percent of firms are privately owned,
- 15 percent are subsidiaries of other companies, and
- the majority of companies employ fewer than 135 persons with one in three companies employing an average of 50 persons or less.[6]

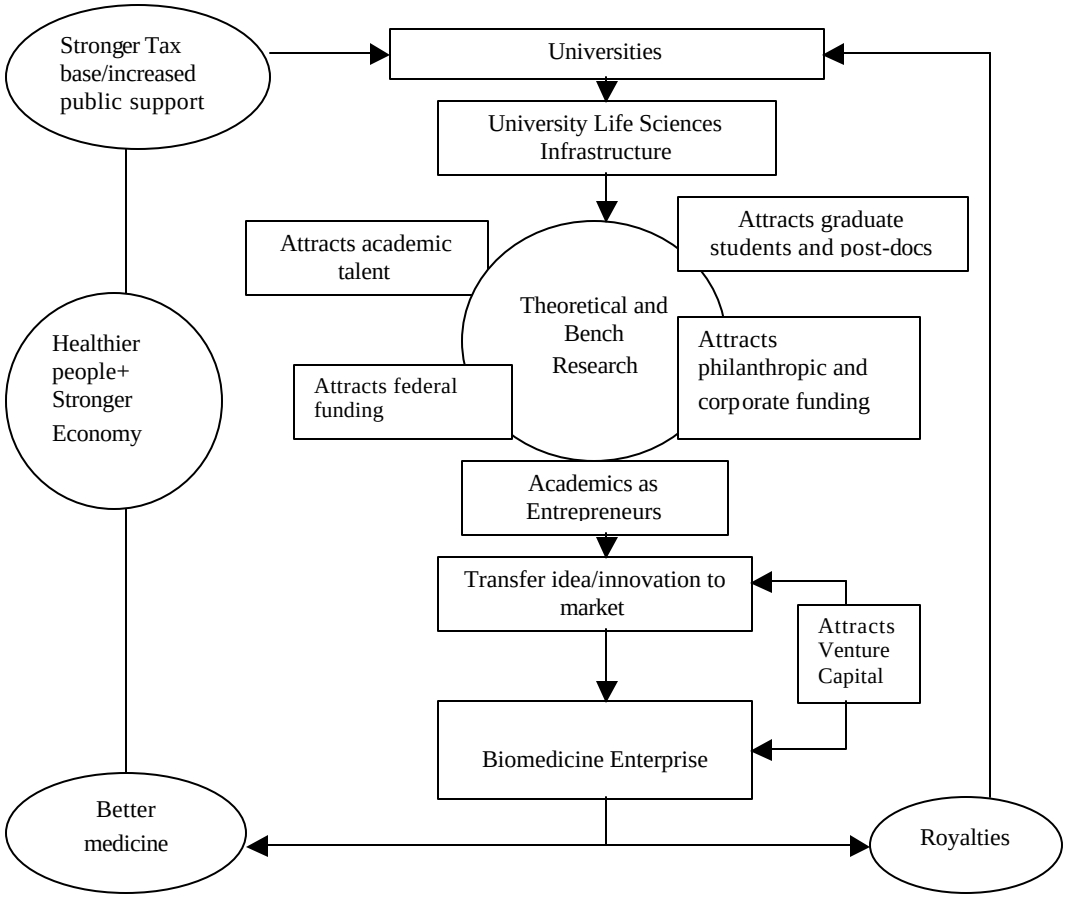
Over the years, many biomedicine companies have become "upstream" R&D channels for the large, multinational pharmaceutical companies. They do so because the latter have (1) the internal capacity for managing the range of clinical and regulatory processes, (2) substantial financial wherewithal of their own, and (3) sophisticated marketing capability.

> A new trend has emerged, however, where numerous biotech companies have sufficient monetary and human capital to independently develop some or all of their investigational drugs. As a result, an increasing number of biotech firms will directly market or co-promote their discoveries, thereby receiving a significantly greater share of product sales and earnings.[7]

1.2.3. *University Connection*

The developmental model commonplace in the industry weds (1) university-based science underwritten in part with federal support, (2) sweat equity by academics and independent scientists as founders or early principals in fledgling companies, and (3) the significant financial risk of non-scientists who bring capital and business know-how to the venture. Figure 1 is illustrative.

Figure 1: University-Biomedicine Industry Relationship



From the university perspective, links to the marketplace are well established and respected today. But just a few decades ago, much of academe considered these ties unseemly at best and inimical to independent scholarship. Over the years, sentiments have changed with campus-business collaboration becoming important for very practical reasons. At an international conference on the university-industry-government relationship, a professor put it this way:

> The increasing demand for funds from universities and research institutes gets a similar response worldwide: support yourselves! That is to say, connect yourselves with industries and the government; offer your knowledge and your capacity to generate new knowledge and charge for it. Only in this way will you be able to extend your laboratories, hire young people, and increase your salaries.[8]

1.2.4. *Needs*

Taking an innovation from the research bench to the market is a long, uncertain, and daunting process. Success depends on the long-term commitment of persons willing to risk-take. The industry can be a voracious consumer. Biomedicine companies at every stage of their growth have on-going need for

- Intellectual Talent,
- Capital,
- Patient Investors, and
- Management Acumen.

Intellectual Talent

The "raw material" of biomedicine, intellectual talent, is a commodity most abundant at the university. Opportunities multiply when the interests of talented graduate students, post-docs, and faculty dovetail with those of business.

> There is a myth that is widely held among scholars, as well as among laypersons, that "science" and "technology" define two quite separate and different cultures. Science is what academics do, and scientists openly publish and otherwise communicate their findings. Technology is what business firms or profit-oriented private inventors do, and they patent their successes. There is a related myth that the relationship between science and technology is one where technologists draw freely on public science that was created with no notion at all as to its likely uses in the development of technology. The problem with these two myths is that they are largely myths. In fact, the worlds of science and technology are, in many fields, closely intertwined. Much of "science" is done with the express purpose of illuminating various areas of possible "technology" development…The intertwining of science and technology is particularly prevalent…in the arena of medical research and innovation. [9]

Capital

Forecasting when a technology is ready for the leap from laboratory to commercial applications is imprecise and always costly. On average, biomedicine companies earmark 50 percent of their revenues to R&D, a level of investment considerably greater than most U.S. industry groups. Because of the huge cost of innovation – a typical new pharmaceutical may require a 7-9 year R&D horizon and consume $400 million – only the largest firms can continue to keep devising new products and putting them through the uncertainties of years-long development.

> For much of the past two years, as other technology sectors collapsed, biotech stocks remained buoyant and investment money flowed because investors believed that biotechnology was different. While telecom firms suffered from a glut of bandwidth and dot-coms struggled to find profitable business models, the market for new medicines appeared limitless.[10]

Patient Investors

Biomedicine R&D is expensive and requires stable and adequate financing. It also requires investors who recognize the risk of R&D and have the patience to wait. Funding mechanisms include

- Debt financing: personal contacts, loans and credit;
- Equity financing: angel investors, venture capitalists, corporate investing/investment banking and public offerings;
- Grants: state, federal, and private philanthropic;
- Mergers and acquisitions;
- Partnerships – with or without equity stakes.

Management Acumen

Shepherding the scope of activity required during R&D, manufacturing and marketing is a significant management challenge. It requires managers with regulatory approval process experience, a thorough understanding of R&D, the ability to structure a work environment conducive to "doing science," and the know-how to build shareholder value.[11]

A pervasive problem in small and middle-sized companies is the shortage of experienced management. "Founding members and key staff of small and medium-sized companies are often particularly qualified for the scientific discovery and development portion of the product cycle, but not for the entrepreneurial and management issues involved in later stages. More often than not, a management team will have to be brought on for specific talents. Attention to fiscal responsibility, investor relations, and staff management are often items that the founders of smaller companies have little interest or skills in being involved with on a daily basis, as time spent managing detracts from time spent conducting innovative research" [12]

Bioinformatics: The use of computers in solving information problems in the life sciences; mainly, it involves the creation of extensive electronic databases on genomes, protein sequences, etc. Secondarily, it involves techniques such as the three-dimensional modeling of biomolecules and biologic systems. (Source: *BioTech Life Science Dictionary.* Copyright BioTech Resources and Indiana University, 1995-98. Accessed on-line at http://biotech.icmb.utexas.edu)

Proteomics: The scientific study of an organism's proteins and their role in an organism's structure, growth, health, disease (and/or the organism's resistance to disease, etc.). Those roles are predominantly due to each protein molecule's tertiary structure/conformation. (Source: Kimball R. Nill. Glossary of Biotechnology Terms. Technomic Publishing Company, Inc., 2001. Accessed on-line at http:// biotechterms.org)

Nanotechnology: From the Latin *nanus* which means dwarf, so it literally means "dwarf technology." The word was originally coined to refer to high precision machining. However, it was later used to refer to a new and developing technology in which man manipulates objects whose dimensions are approximately 1 to 100 nanometers. (Source: Kimball R. Nill. Glossary of Biotechnology Terms. Technomic Publishing Company, Inc., 2001. Accessed on-line at http:// biotechterms.org)

1.2.6. *Markets*

The historic market for the biomedicine industry is medical therapeutics and diagnostics. However, because many processes and products have dual use potential, biomedicine/tech products find their way into sectors as diverse as veterinary medicine, agriculture, and waste management. The industry is also experiencing the convergence of biomedicine and non-biotech high technology. Convergence creates hybrid products such as structures that self-assemble, molecular electronics and even "biocomputers."[13] The convergence of biology and information technology is also creating new industry segments (see sidebar above) such as bioinformatics, proteomics, and medical nanotechnology.[14]

> Today, agriculture and healthcare biotech are at the core of what the industry does. There are lots of exciting things happening in those areas that enhance life. But NASA is working on systems that attempt to mimic processes in the biological world. When we send probes to space, we will try to give them lifelike properties. We want them to be robust, self-reliant, adaptable, and evolvable, to heal when damaged, with complete self-awareness.… Biotech and biology will be

the hallmarks of the 21st century. The rapid development of the silicon era led to rapid growth of companies such as Intel. The upcoming revolution in biotech will propel other companies as America starts populating other planets. It will be an exciting odyssey and I am confident it will return benefits out of this world. Our grandchildren will be grateful for the work the biotech industry did today, creating biology-inspired products that will dramatically improve quality of life on earth. Daniel S. Goldin, Former NASA Administrator.[15]

1.2.7. *Forecast*

The biomedicine industry, while not entirely recession proof, has tremendous economic momentum and upside. The 377 publicly owned biotechnology companies had a reported market value of $441 billion at the end of 2000. The federal government estimates that biotechnology will account for16 percent of the nation's GDP -- $8,700 per person annually—by 2010. Although growth seems certain, "predicting which technologies will make it out of the lab is exceptionally difficult…it is certain that advances in understanding the genetic basis of disease will significantly increase the number and efficacy of both diagnostic tools and therapies. And this flood of innovation will affect the cost and delivery of services."[16]

Growth in the industry expected throughout this decade will likely stimulate:

1) Increased diagnostic efficacy—the nation now spends about $40 billion annually on diagnostic laboratory-related work. Because 70% of medical treatment decisions are based on diagnostics, improved diagnostics means more demand for medical services and, with it, increased costs.
2) Increased Consumer demand for the new and better.
3) Increased shift from labor-intensive medicine (nurses, physicians) to capital-intensive medicine (drugs, devices).
4) Increased delays in FDA approval times (and with it increased costs) as the limited capacity of the FDA to process and monitor clinical trials applications is overloaded as new products back up awaiting FDA examiner attention. (Waiting out this extended process is difficult for inadequately capitalized smaller companies.)
5) Increased benefits to academic medical centers and clinical research organizations as demand for clinical trials increases.
6) Increased consumption of lifestyle drugs such as Botox and Viagra.
7) Increased longevity because new biomedicines will treat disease causes rather than symptoms.
8) Increased shift to disease management.
9) Increased capability for tailoring therapies to individual consumer need.
10) Increased R&D costs (research-based drug companies now spend 20% of profit on R&D), and,
11) Increased government and HMO pressures to contain costs can squeeze profit margins causing venture capital to leave the industry.[17]

2. Strengths in California

2.1. Overview

California has been a worldwide hub for biomedical research and development for three decades. Key milestones in the industry have California origins:

- 1973—Stanford geneticists and UCSF biochemists publish seminal article about using DNA to make first recombinant organism;
- 1978—Genentech and City of Hope develop and demonstrate first angioplasty system;
- 1983—UCSF scientist isolates the AIDS virus;
- 1987—Hepatitis C virus cloned by Chiron scientists;
- 1989—Amgen recombinant DNA product for kidney failure approved by FDA;
- 1992—First coronary stent developed at Scripps Clinic, San Diego (jointly with scientist at the University of Texas);
- 1999—Elan Pharmaceuticals, South San Francisco, demonstrates use of protein drug as possible treatment for Alzheimer's disease.[18]

The biomedicine industry is knowledge-driven. The process has been and continues to be enabled by decades of federal research funding. California is a magnet for National Institutes of Health (NIH) and other federal support. Considering NIH only, in 2000 university- and industry-based biomedicine researchers statewide received nearly $2.3 billion. NIH contract and grant awards totaled more for California than any other state and were almost 40 percent greater in 2000 than in 1996.[19] The trend continues today.

The biomedicine industry flourishes in California because of the:

- Willingness of individuals, governments and business to risk-take;
- Productivity and wealth-producing reality and potential of the industry; and
- Comfort level California's biomedical industry has in venturing and collaborating with partners worldwide.

2.2. Impact

The biomedicine industry's highly paid employees mean an increasing tax base and increasing property values. The industry also has broad, collateral impact on businesses as varied as retailing, real estate, construction, and communication.

The biomedicine industry in California has grown from a handful of companies in the mid-1970s to more than 2,500 today. In 2000, California biomedicine received about 45 percent of venture capital dollars invested in the industry worldwide and earned $7.8 billion in annual revenues. The industry also employed about 225,000 Californians in high-wage jobs. While episodic economic ups and downs and the cul-de-sacs inevitable in scientific discovery typify the industry's brief history, the prognosis virtually every authority agrees on is that the industry has long-term growth potential in California.

2.3. University-Industry Collaboration

California's research universities have national and international reputations in the life sciences. It is not surprising, therefore, that companies that value and need intellectual know-how would choose to locate as close as possible to the "raw material" so essential to their success: intellectual capital. More than 80 percent of California's start-up and established biomedicine companies are relatively close to the major life sciences research universities: Caltech, UC Berkeley, UCSD, UCI, UCLA, UCSF and Stanford.

In turn, the universities look to biomedicine companies for enhanced research, enhanced learning and teaching opportunities, enhanced influence on government and private funders, and for enhanced revenues from the intellectual property originating on their campuses.

California higher education and biomedicine are tied in ways that strengthen both. Examples include:

- CSUPERB (California State University Program for Education and Research in Biotechnology): $1 million fund to underwrite joint ventures between campus-based researchers and private sector life sciences companies.
- The Biostar Project: biotech companies co-sponsor research projects at UC. The university and partnering companies share results; $46.7 million invested in 177 research projects as of 2000.
- UC Life Sciences Informatics: housed at UC Davis, the program, co-sponsored by UC and biomedical companies, funds convergence projects involving the life sciences, mathematics, statistics, engineering, and computer sciences.
- Mission Bay: UC San Francisco is developing a 43-acre, $1.4 billion satellite campus for bioscience research.
- California Institutes for Science and Innovation: This program is a unique partnering of the State, industry and UC; it builds on the existing biomedicine resource infrastructure in the seven clusters statewide to encourage specialized convergence initiatives.
- CONNECT: established by UCSD, the CONNECT process brings entrepreneurs, researchers, and business together to create social networks that facilitate the growth of biomedicine and other high tech-companies.

2.4. Employment

The industry reports more than 2,500 healthcare technology companies and 87 universities and private non-profit research organizations engaged in basic and applied biomedical research and development in California in 2002. Statewide employment by industry sector is depicted below.

Table 1: Employment by Industry Sector in California[20]

Industry Sector	Number of Employees
Medical Device and Instrument Manufacturing	76,000
Biopharmaceuticals	72,000
Academic Research	40,500
Wholesale Trade	29,250
Laboratory Services	6,700

2.5. Distribution

About 80 percent of California's biomedicine industry is located in seven clusters in three regions of the State: Northern and Southern California and San Diego County. Table 2 identifies employment within the regions and within sub-regional clusters.

Table 2: Distribution of Biomedicine Companies and Employees by Cluster

Clusters	Number of Companies	Number of Employees	Mean No. Employed per Company	Major Research Universities, Academic Medical Centers, Research Organizations
1. San Francisco Bay Area Cluster	645	80,000	124	UCSF, UC Berkeley, UC Santa Cruz, Stanford
2. Sacramento Cluster	102	4,600	45	UC Davis
Northern California Total[21]	747	84,600	113	
3. Los Angeles County Cluster	467	35,000	75	UCLA, USC, Charles Drew University, City of Hope, Cedars Sinai, Caltech
4. Orange County Cluster	337	33,000	99	UC Irvine
5. Riverside-San Bernardino Counties Cluster	101	3,400	33	UC Riverside, Loma Linda University
6. Santa Barbara-Ventura Counties Cluster	134	8,400	62	UCSB
Southern California Total[22]	1,039	79,800	77	
7. San Diego County Cluster	401	27,000	67	UCSD, Salk Institute, Burnham Institute, Scripps Research Institute
San Diego County Total[23]	401	27,000	67	
Total for Seven Clusters	2,187	191,400	87	
Total Statewide	2,500	225,000	90	

Industry observers expect growth in the clusters to continue in the coming years as new medical equipment, drugs, and therapeutics move from research into marketing channels. A 2002 report about the industry not only suggests that clustering in the industry is a good thing, but that industry leaders should encourage it because the collaboration of scientists, entrepreneurs, venture capitalists, suppliers, and service providers creates synergy.[24] http://www.chi.org/pdf/chi_Survey_2002_SOCAL

2.6. Economic Activity

In 2001, the industry was robust despite the emerging recession. Table 3 depicts selected industry activity in the three regions.

Table 3: Biomedicine Industry Economic Activity in Three Regions

	Southern California[25]	Northern California[26]	San Diego County 1999[27]
Total Number of Biomedical Companies	1,039—2,090[28]	819	500
Total Worldwide Revenues	$3.7 billion	$4.1 billion	N/A
Total Employees	79,800—125,155	84,600—85,949	27,000—30,000
Total Reported Private Investment in R&D	$852 million	$1.1 billion	$1.21 billion
Total Exports	$3.7 billion	$2.7 billion	$1.7 billion
Total Wages and Salaries Paid	$6.4 billion	$5.8 billion	$1.5 billion
Total NIH Grants Awarded	$1.4 billion	$893 million	$627 million (non-classified R&D)

2.7. Industry Snapshot

Table 4 is a composite snapshot of the industry based on recent data from a variety of sources.

Table 4: Biomedicine Industry California Snapshot

Factors	Snapshot
Businesses	2,500 companies[29]
Employment Industry-wide	225,000[30]
Annual Salary and Wages (based on 212,000 employees)	$13.7 billion in 1998[31]
Average Salary Industry-wide	$64,353 exclusive of other financial remuneration 2000[32]
Industry Sales	$20+ billion with 71% of revenue from product sales[33]
Private Investment	$2.1 billion in 2000[34]
Revenues Invested by Industry Companies	45% of operating expenses[35]
Exports (a)	$6.4 billion[36]
Federal R&D Investment Industry-wide (b)	$14.4 billion in 1999[37]
Federal Health and Human Services R&D investment	$1.4 billion[38]
Charitable Support	$170 million in 1998[39]
Industry R&D Investment (c)	$852 million in 2000[40]

(a) Type of exports:
surgical and medical equipment, 50%
bio-pharmaceuticals, 28%
laboratory equipment, 22%
(b) Non-classified grants and contracts
(c) The biomedicine industry invests four times more in research and development than do other high-tech industries

2.8. Regional Detail

2.8.1. *Southern California Region*

Medical devices—surgical , medical devices, and lab equipment—make up nearly two-thirds of the industry's Southern California exports.

The region's large biomedical companies are expanding. The founder of Medtronic MiniMed, with 1,600 employees at its 28-acre facility at the California State University, Northridge campus, recently announced multimillion-dollar gifts to both UCLA and USC to further their capacity for life sciences research. Similarly, Baxter recently invested more than $500 million to expand and upgrade its bioscience facilities near Amgen in Thousand Oaks. Southern California's biomedical industry paid more than $6.4 billion in wages and salaries in 2000, with salaries averaging $50,800. The typical Southern California biomedicine company invested 40 percent of operating revenues in R&D in 2000. The area also receives more federal research dollars for biomedicine than any other region.[41]

Governments as well as various private organizations are collaborating to spur growth of the biomedicine industry in the region by identifying potential funding, office space and other elements that contribute to nurturing any new business. The City of Los Angeles, for example, is working with developers in the San Fernando Valley, San Pedro, and LAX area to construct buildings expressly for biomedical business needs. Similarly, the City of Pasadena is encouraging development in a corridor that includes the Huntington Memorial Hospital, the Jet Propulsion Lab, and Caltech.

Despite the fact that Southern California leads the nation in public and private research dollars and in the value of its exports, the area has few large biomedicine companies. The relative lack of large companies explains why the region does not have a reputation as a center for biomedicine. The lack of larger companies also means that new biosciences graduates tend to look elsewhere in California or nationally for employment. These factors also contribute to the relative difficulty companies in the region have in attracting venture capital.[42]

2.8.2. *Northern California Region*

Two of the ten top NIH grant recipient institutions in the nation are located in Northern California: UCSF and Stanford. A 2000 survey found that 33 percent of biomedical companies in Northern California credit universities and private independent research organizations with being instrumental in their evolution. Forty-two percent report on-going research agreements with academic or related institutions, and about 30 percent have active patent license agreements with such organizations.[43]

For instance, in South San Francisco, the historic home of the industry in the region and statewide, the number of biomedicine/tech firms doubled between 1995 and 2000. Today the area's 51 firms employ 6,100 with an additional 1,000 jobs expected to be added in 2003. Biomedicine/tech companies make up 5 of the 12 largest employers in South San Francisco. "According to City of South San Francisco data, nearly one in every three workers in the sections of South San Francisco east of Highway 101 is employed at a local biotech or medical device company."[44] Industry businesses currently occupy 2.5 million square feet of office, laboratory, manufacturing, and warehousing space. Projected growth is expected to double the investment in real estate and construction in 2003. [45]

Biomedicine is also growing elsewhere in the region including in the cradle of high-tech.

> Silicon Valley's hi-tech industry may be languishing in the doldrums, but the seeds of the next boom have already been planted. Many industry observers believe that biotechnology will lead the next revolution, transforming the way drugs are developed and leading to fundamental breakthroughs in medical treatment and research.[46]

In Northern California, medical devices, instruments and diagnostics, and biopharmaceuticals are the major employers in the industry, followed by academic research and wholesale trade.[47] The Bay Area is particularly competitive in biopharmaceuticals and medical devices because of the extensive complementary technology industries in the area such as microelectronics, telecommunications, biotechnology, and software development. Fully 42 percent of California's biomedicine/tech exports are processed through the San Francisco customs district.

2.8.3. *San Diego Region*

Employment in the industry in this region is estimated at 125,000.[48] About one in three work in biopharmaceuticals or medical device design and manufacture, one in three in instrument and diagnostic tool design and manufacture, and one in five in academic research, industry-related wholesaling, and laboratory or industry support services.

The tie between the industry and the university community is dramatically evident in San Diego County. Many of the world's major biomedical research organizations are located within a few miles of one another and the UCSD Torrey Pines campus. In addition to the UCSD School of Engineering, School of Medicine, Department of Biology, and Center for Wireless Communications, the cluster includes the Salk Institute for Biological Studies, Scripps Research Institute, Burnham Institute, Sidney Kimmel Cancer Center, Neurosciences Institute and the La Jolla Institute for Allergies and Immunology. Biomedicine R&D in San Diego received nearly ten percent of the $14.4 billion in federal non-classified research dollars California received in 1999.[49] The amount of federal investment in San Diego R&D biomedicine is particularly noteworthy because the investment is concentrated in one county rather than in a multi-county region. After Los Angeles County, San Diego County was the next largest recipient of federal R&D funding in California in 2000.

San Diego County is home to about 500 biomedical companies serving various markets: 44% biopharmaceuticals; 25% medical devices, instruments and diagnostic tools development and manufacture; 22% academic research; 7% wholesale trade; and 2% laboratory services. Salaries and wages in the industry in the San Diego cluster averaged nearly $54,000 in 2000.

The area has also become home in recent years to an influx of "Big Pharma" (global pharmaceutical companies) attracted by the biotech, medical device and diagnostics businesses there. Companies such as Shering-Plough, Johnson & Johnson, Novartis, and Merck have significant investments in the region in joint ventures, strategic alliances, contracted research, and licensing and royalty arrangements with local companies.

The biomedical industry in San Diego invests 51 percent of operating funds in research and development, fully four times more in research and development than other high technology industries.[50]

2.9. Investment and Financing

A number of private, non-profit, and government organizations collaborate in promoting the industry by identifying potential funding, potential facilities, partnering organizations and the many other things needed to nurture new business. Interest in the industry surged virtually overnight following the 1980 U.S. Supreme Court determination that genetically altered life was a patentable commodity.[51] Since 2000, California has received about 45 percent of the worldwide venture capital dollars invested in the industry:

- biopharmaceuticals, $1.5 billion,
- medical devices, $1.16 billion, and
- medical information services, $769 million.

The large, multinational pharmaceutical companies invested more than $2.5 billion in California in 2000 through various mechanisms including joint ventures, licensing and royalty arrangements, and strategic alliances. Public documents report 275 collaborations

between large pharmaceutical companies and California biotechnology firms in 2000 alone. [52]

The industry is expected to grow significantly in the coming years as an increasing number of new biopharmaceutical and medical technology products move from the lab to markets. The biomedical industry is supported by one of the nation's most educated workforces, world-class research universities and California's long history of innovation and entrepreneurial initiative.

2.10. Research & Development

A recent survey found that although the typical California biomedicine company invests 45 percent of its operating expenditures in R&D, less than half of companies generated revenues and had products in the marketplace. Research and then testing to demonstrate efficacy are requisite steps, but the process has inherent challenges. A recent survey of companies reports that of the medical products surviving the rigors of development and testing, only one in three generated revenues greater than their R&D investment in the product.[53]

California's biomedicine companies using informatics and the new sciences of genomics and proteomics are doing leading-edge R&D to increase understanding of health and disease as well as more effective and new treatments. Diseases most targeted by California companies are cancer, cardiovascular disease, and infectious diseases including AIDS/HIV, diabetes, and respiratory disease. Notable R&D underway today in each of the state's industry clusters involves stem cell, cloning, Alzheimer's disease, and antibody research.[54]

3. Weaknesses

3.1. Smaller Companies

An on-going problem the industry faces, particularly the small and medium-sized companies, is lack of ability to attract needed, highly skilled, intellectual talent. Although California's public and private universities graduate more Masters and Doctoral degree holders in the life sciences and related disciplines than any other state each year, demand in many communities exceeds supply. Small companies are especially hard-pressed to compete with larger companies for new talent and must look outside of California to find the skilled persons they need. But recruiting talent elsewhere has a number of challenges, not the least of which is the cost of housing in California and fear, usually by their spouses, of earthquakes.[55]

3.2. Venture Capital Investors

Venture capital is essential to R&D. Unfortunately, the R&D process in biomedicine is inherently long-term, while venture capitalists look for "big hits" sooner than later. The uncertainty that products will live up to their theorized potential, coupled with capital-intensive development requirements, likely means that a great many innovations never make the transfer from the lab to the market because they fail to attract venture support.

3.3. Challenges

The industry in California faces considerable challenge in the years to come:

- The Internet: information that only a few years ago was comparatively difficult to obtain is now available worldwide for anyone to access and build upon.

- Communication: finding the most appropriate vehicle for helping scientists, business persons, consumers and policymakers alike to keep up with change happening globally and at an ever accelerating pace.
- Access to capital: biomedicine is capital-intensive with very lengthy R&D requirements. Sustaining companies over long periods will require continued public investment in the form of grants, contracts, tax incentives, and other government action, more risk-taking by entrepreneurs, and more venture capital investment.
- Private investment in public entities (PIPES): mechanisms such as the CSUPERB Joint Ventures Program seek to assure that facilities, equipment, and technology remain state-of-the-art, continue to attract talent and become seedbeds for new innovation.[56]

4. Policy Considerations

More than half of the companies in the biomedicine industry in California were founded in the last ten years and of these, two-thirds are privately owned.

As with any young industry, there are many challenges. To sustain a fertile environment for the industry's success and growth in the 21st century, government policy—on issues such as tax policy, continued funds for public and private university-based research and education, medical records confidentiality, Medicaid and Medicare reimbursement, incentives for R&D, and oversight of research—is critical. Continued dialogue and partnership between public and private sectors will help the industry meet its challenges and fulfill its promise—to continue to push the frontiers of medical technology and healthcare, improve life for generations to come, and create the wealth that will keep the California economy strong.[57]

Issues and Policy Considerations

1) Issue: Although California universities graduate large numbers of life sciences graduates each year, the number of graduate students and post-doctoral students in the employment pool is insufficient to meet the need. Small and medium-sized companies, in particular, have difficulty competing for available employees. In the absence of effective outreach, information about career opportunities, and assistance in bridging the gap between employers and graduates, advanced students will continue to look to larger California companies or out of state for career employment.

Policy Consideration: Improving the competitive ability of California companies and career opportunities for Californians are important public policy objectives. The whole industry in California would benefit from an in-state and out-of-state campaign to recruit life science graduates. The only impediment to continued growth of the industry in California is the lack of a sufficient pool of life science students. This long-term need requires a long-term strategy. To assure sufficient talent in the decades ahead more students must have sufficient science education to ready them for graduate school. Business, school districts, and colleges and universities should be encouraged to collaborate in establishing and supporting science education "pipelines" that provide mentoring, tutoring, and coaching in science and math from the elementary grades through community college.

2) Issue: The industry's growth in California has tended to be greatest in communities proximate to major research universities. This is true for young as well as established companies.

Policy Consideration: Since 80 percent of the industry in California is clustered in areas with major research universities, other parts of the state do not benefit as directly. Biomedicine companies are good neighbors. They add socio-cultural and economic value to their communities and are environment-friendly. Consideration should be given to developing ways of facilitating links between the industry and the 23-campus California State University (CSU) system. Doing so expands the geographic distribution of the industry and has long-term positive consequences for rural and urban California alike.

3) Issue: Stem cell research is important to advancing knowledge and to the creation of new treatment modalities. It is also controversial and politicized. Yet new California law that goes into effect in January 2003 seems to give our researchers a reprieve from federal policy limits to this science.[58]

Policy Consideration: California researchers are nationally recognized for their contributions to Stem Cell research. Scientists from all over the nation will likely be attracted to relocate here should the new California law survive future contravening federal legislation. Using California law to open opportunities for inquiry in this science expands knowledge and holds the promise for effective treatment of Parkinson's disease, Alzheimer's disease, and Cystic Fibrosis among many others. Expansion of Stem Cell research reinforces California's leadership in biomedicine.

4) Issue: Many biomedicine companies have origins in work first explored in university laboratories. Companies and universities recognize the value of such intellectual property contribution with various types of royalty fees and other arrangements. These arrangements, however, mask other important outcomes such as increased tax revenues, increased employment, and increased property values as a result of work "seeded" by the university. Inflexible royalty requirements, on the other hand, can sour company-university ties and discourage out-of-state companies from choosing California universities as their research partners. In other words, patent and other royalty arrangements that discourage investors may ultimately be more costly to the universities, their communities and the State of California than the fees they actually generate.

Policy Consideration: The mechanisms the UC and CSU use to protect intellectual property may discourage off-campus enterprise. The cost-benefit of existing mechanisms should be considered.

5) Issue: Government regulation and tax codes sometimes have unintended consequences for biomedicine R&D. Structured appropriately, though, they can be used to stimulate discovery in targeted research sectors and/or to encourage companies to locate in "high need" locales.

Policy Consideration: The impact of tax laws intended to encourage productive investment in capital assets or to encourage companies to locate in "biotech corridors" or specific locales, for example, should be considered.

6) Issue: Each innovation in the biomedicine R&D pipeline has potential demand- and supply-side impact. Television advertising is demonstrably effective in increasing prescription drug sales. So is the marketing to provider end-users of new "indispensable" drugs or medical devices.

Policy Consideration: Innovations in biomedicine can be lifesaving and life enhancing. They also have potential for taking investment and health care dollars away from other equally compelling needs. Consideration of these trade-offs is a must for policymakers.

7) Issue: The biomedicine industry and publicly sponsored research are intertwined. The federal government underwrites a huge part of discovery costs. So does the use of public university facilities and talent. Should private ownership rights come from publicly funded research? Should the private firms that own patents for products developed with public money have the right to charge anything they want for the product? Should profits inure solely to the developers of a drug developed with public funds?

Policy Consideration: Private investors expect to be rewarded for their investment. Why shouldn't government? Consideration of how a return on public investment should be calculated and what constitutes a fair return is needed.

Selected Resources[59]

Periodicals

Annual Biotechnology Industry Report
www.burrillandco.com

BioCentury: The Bernstein Report on BioBusiness
www.biocentury.com

BioWorld Today, BioWorld Week, and BioWorld Biotechnology State of the Industry Report, www.bioworld.com

Biospace.com
www.biospace.com

FDC Reports: The Pink Sheet
www.fdcreports.com

Genetic Engineering News
www.genengnews.com

MedAdNews
www.pharmalive.com

Nature Biotechnology
www.nature.com/nbt

PharmaBusiness
www.pharmalive.com

Signals: The online Magazine of Biotechnology Industry Analysis, Recombinant Capital
www.recap.com

Trade Associations

The Biotechnology Industry Organization
www.bio.org

Pharmaceutical Research and Manufacturers of America
www.phrma.org

Strategic Information about the Industry

Tufts Center for the Study of Drug Development
www.tufts.edu/med/csdd

ENDNOTES

[1]Determining what the industry actually represents is problematic because industry and governments use different criteria to characterize it. Some in the industry use federal definitions, others use definitions by other levels of government. Agencies from the IRS to the Interstate Commerce Commission and Food and Drug Administration classify industry and enumerate companies based on *what* they produce or provide rather than *how* they produce it. The federal government defines *biotech*, for example, as activities "that use organisms or their cellular, subcellular, or molecular components to make products or modify plants, animals, and micro-organisms to carry desired traits" to treat disease. See Jon Paugh and John C. Lafrance, "Meeting the Challenge: U.S. Industry Faces the 21st Century – The U.S. Biotechnology Industry," U.S. Department of Commerce, Office of Technology Policy, July 1997, p. 9.

[2]The California Trade and Commerce Agency, in a more focused definition, says that biotech "relies on living organisms or biological systems…to make products that were formerly nonexistent, or rare and expensive. Biotechnology includes research into genetics and chemical processes that take a discovery and translate it into the relief of suffering." See Office of Economic Research, California Trade and Commerce Agency, Office of Economic Research, *Biotechnology*, May 2001, p 1.

[3] Loet Leydesdorff and Henry Etzkowitz, October 1996 "Emergence of a Triple Helix of University-industry-government relations," *Science and Public Policy*, v. 23, no. 5, pp. 279-286; Henry Ezkowitz and Loet Leydesdorff. 1997, Universities *and the Global Knowledge Economy: A triple helix of university-industry-government relations*, (London and Washington: Pinter), pp. 85-96.

[4] Victor W. Hwang, Rohit K. Shukla (eds), 2001, *Heart of Gold: The Bioscience Industry in Southern California*, Larta, p.14. http://www.larta.org

[5] *New York Times*, June 18, 1996.

[6] Jon Paugh and John C. Lafrance, "Meeting the Challenge: U.S. Industry Faces the 21st Century – The U.S. Biotechnology Industry," U.S. Department of Commerce, Office of Technology Policy, July 1997, p. 10.

[7] Industry Trends, "New Paradigms in Cancer Therapeutics," *Biotechnology Industry Survey*, V.1 A-D, (December 20, 2001) pp. 10-11.

[8] Henry Ezkowitz and Loet Leydesdorff. 1997, *Universities and the Global Knowledge Economy: A triple helix of university-industry-government relations*, (London and Washington: Pinter), pp. 85-96.

[9] Nelson, Richard, "The Intertwining of Public and Proprietary in Medical Technology;" In: Nathan Rosenberg, Annetine C. Gelijns, and Holly Dawkins (eds), 1995, *Sources of Medical Technology: Universities and Industry. Medical Innovation at the Crossroads*, Volume V, Committee on Technological Innovation in Medicine, Institute of Medicine. Washington, D.C.: National Academy Press, pp. 219-20.

[10] Terence Chea, "Companies Re-tool Strategies To Survive Investment Slump," *ThechNews.com (June 26, 2002) page E01.*
Http://biotech.about.com/gi/dynamic/offsite.htm?site=http%3A%2F%2Fwww.washingtonpost.com%2Fwp-dyn%2Farticles%2FA44759-2002Jun25.html

[11] Victor W. Hwang, Rohit K. Shukla (eds), 2001, *Heart of Gold: The Bioscience Industry in Southern California*, Larta, p.5. http://www.larta.org

[12] Ibid, 27.

[13] *Convergence: the Biotechnology Industry Report*, Ernst & Young, Millennium Edition, 2000, SCORE Retrieval File No.000254. pp. 12-30. www.ey.com

[14] *Biomedicine: The Next Wave for California's Economy: 2002 Report on California's Biomedical R&D Industry,* La Jolla: California Healthcare Institute/PricewaterhouseCoopers, www.chi.org/pdf/chi_2002_pdf

[15] *Biotech Star Wars*, BioSpace Inc., http://www.biospace.com/articles/010600_Dan.cfm

[16] Douglas I. Kalish and Geoffrey S. Thompson, Second Quarter 2002, "The Biotech Explosion", *The Milken Institute Review*, Second Quarter 2002, p. 22.

[17] Ibid, 22-31.

[18] California Healthcare Institute Millennium Report: *Report on California's Biomedical R&D Industry*, (Undated), www.biospace.com/b2/chi_2000.cfm

[19] *Biomedicine: The Next Wave for California's Economy: 2002 Report on California's Biomedical R&D Industry,* La Jolla: California Healthcare Institute/PricewaterhouseCoopers, www.chi.org/pdf/chi_2002_pdf

[20] Ibid, 15.

[21] *Biomedicine: The New Pillar in Northern California's Economy*, La Jolla: California Healthcare Institute/PricewaterhouseCoopers. www.chi.org/pdf/chi_Bayarea_2002.pdf

[22] *Biomedicine: The Next Wave for Southern California's Economy*, La Jolla: California Healthcare Institute/PricewaterhouseCoopers, www.chi.org/pdf/chi_Survey_2002_SOCAL

[23] *2002 California Biomedical Industry Highlights*, LaJolla: California Healthcare Institute, www.chi.org/sandiego_facts.php

[24] *Biomedicine: The Next Wave for Southern California's Economy*, La Jolla: California Healthcare Institute/PricewaterhouseCoopers, www.chi.org/pdf/chi_Survey_2002_SOCAL

[25] Ibid.

[26] 2002 Report on Northern California's Biomedical R&D Industry, La Jolla: California Healthcare Institute/PricewaterhouseCoopers, www.chi.org/pdf/chi_Bayarea_2002.pdf

[27] *2002 California Biomedical Industry Highlights*, LaJolla: California Healthcare Institute, www.chi.org/sandiego_facts.php

[28] Sources differ on the actual number of companies in the Southern California area; therefore, a range of estimates is provided.

[29] *Biomedicine: The Next Wave for California's Economy: 2002 Report on California's Biomedical R&D Industry.* La Jolla: California Healthcare Institute/PricewaterhouseCoopers, p. 2. www.chi.org/pdf/chi-2002.pdf

[30] Ibid, 3.

[31] California Healthcare Institute Millennium Report: *Report on California's Biomedical R&D Industry*, (Undated), p.3 www.biospace.com/b2/chi_2000.cfm

[32] *The Next Wave for California's Economy: 2002 Report on California's Biomedical R&D Industry* La Jolla: California Healthcare Institute/PricewaterhouseCoopers. 15 www.chi.org/pdf/chi-2002.pdf

[33] California Healthcare Institute Millennium Report: *Report on California's Biomedical R&D Industry*, p.2 www.biospace.com/b2/chi_2000.cfm

[34] Ibid, 6.

[35] *The Next Wave for California's Economy: 2002 Report on California's Biomedical R&D Industry* La Jolla: California Healthcare Institute/PricewaterhouseCoopers. 6. www.chi.org/pdf/chi-2002.pdf

[36] Ibid,12.

[37] Mary L. Walshok, Edward Furtek, Carolyn W.B. Lee, and Patrick H. Windham, "Building Regional Innovation Capacity," Industry & Higher Education, February 2002, 27-42.

[38] Ibid.

[39] California Healthcare Institute, Industry Facts: 2002 California Biomedical Industry Highlights. www.chi.org/facts.php

[40] Ibid.

[41] CHI/PricewaterhouseCoopers, Biomedicine: The Next Wave for Southern California's Economy: 2002 Report on Southern California's Biomedical R&D Industry. www.chi.org/pdf/CHI_Survey_2002_SOCAL

[42] Victor W. Hwang, Rohit K. Shukla (eds) Heart of Gold: The Bioscience Industry in Southern California, 2001, Larta, p.7. http://www.larta.org

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[47] California Healthcare Institute, PricewaterhouseCoopers. Biomedicine: the New Pillar in Northern California's Economy, 2002 Report on Northern California's Biomedical R&D Industry. 5-9. www.chi.org/pdf/chi_Bayarea_2002.pdf

[48] CHI, 2002 California Biomedical Industry Highlights, www.chi.org/sandiego_facts.php

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[50] California Healthcare Institute/PricewaterhouseCoopers. 2002 Biomedical Industry Highlights: San Diego County. www.chi.org/LAOC_facts.php

[51] Cynthia Robbins-Roth, "From Alchemy to IPO: The Business of Biotechnology", 2000 Perseus Books, BioSpace. www.biotech.about.com/gi/dynamic/offsite.htm?site=http%3A%2F%2Fwww.biospace.com%2Farticles%F010600.cfm

[52] CHI/PricewaterhouseCoopers, "Biomedicine: The Next Wave for California's Economy: 2002 Report on California's Biomedical R&D Industry." 6 www.chi.org/pdf/chi-2002.pdf

[53] Ibid, 10.

[54] Ibid, 25-27.

[55] Ibid, 27.

[56] Steven Burrill, "The Biomedical Industry Has Arrived." In: CHI/PricewaterhouseCoopers, Biomedicine: The Next Wave for California's Economy: 2002 Report on California's Biomedical R&D Industry.9 www.chi.org/pdf/chi_2002.pdf

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