An Analysis of the Role of Government in the Locational Decisions of Cambridge Biotechnology Firms

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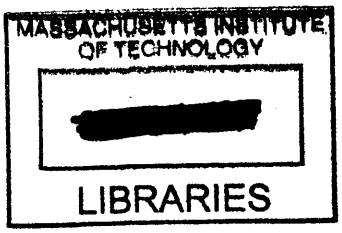

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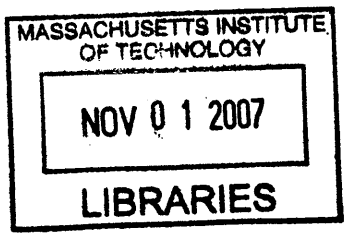

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Part I: Foundations

...the US has always had an active state industrial policy, just like every other industrial country. It's been understood that a system of private enterprise can survive only if there is extensive government intervention. It's needed to regulate disorderly markets and protect private capital from the destructive effects of the market system, and to organize a public subsidy for targeting advanced sectors of industry, etc.

But nobody called it industrial policy, because for half a century it has been masked within the Pentagon system. Internationally, the Pentagon was an intervention force, but domestically it was a method by which the government could coordinate the private economy, provide welfare to major corporations, subsidize them, arrange the flow of taxpayer money to research and development, provide a state guaranteed market for excess production, target advanced industries for development, etc. Just about every successful and flourishing aspect of the US economy has relied on this kind of government involvement.

...Japan and Germany and every functioning economy -- namely, rely on government initiatives to provide the basis for private profit. In the periphery of Japan -- for example in South Korea and Taiwan -- we've been seeing a move out of the Third World pattern to an industrial society through massive state intervention.

You have to remember that what's called military industry is just hi-tech industry. The military is a kind of cover for the state sector in the economy. At MIT where I am, everybody knows this except maybe for some economists. Everybody else knows it because it pays their salaries. The money comes into places like MIT under military contract to produce the next generation of the hi-tech economy. If you take a look at what's called the new economy - computers, internet - it comes straight out of places like MIT under federal contracts for research and development under the cover of military production. Then it gets handed to IBM when you can sell something.

At MIT the surrounding area used to have small electronics firms. Now it has small biotech firms. The reason is that the next cutting edge of the economy is going to be biology based. So funding from the government for biology based research is vastly increasing. If you want to have a small start-up company that will make you a huge amount of money when somebody buys it someday, you do it in genetic engineering, biotechnology and so on. This goes right through history. It's usually a dynamic state sector that gets economies going.[1]

--Noam Chomsky

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[1] http://www.thirdworldtraveler.com/Chomsky/ChomOdon_GlobEcon.html and http://www.zmag.org/content/showarticle.cfm?ItemID=2804

Introduction

The aforementioned comments by Prof. Noam Chomsky of MIT stand in stark contrast to the conventional wisdom that commercial decisions in industry are driven solely by market forces and that economic development, whether it occurs domestically or internationally, is solely the function of private enterprise and the "entrepreneurial spirit" that is celebrated as part of America's individualist ethos. Yet, aside from the "out-of-the mainstream" viewpoints expressed by dissident scholars such as Chomsky, the actual role that government plays in economic development has seldom been put to the test. This is especially true at a time when knowledge-intensive technologies such as aerospace, the Internet, and biotechnology are all having such a huge impact upon economic development. However, these are each also technologies in which the argument can be made that government has played a critical role as a market (aerospace); infrastructure developer (Internet); and both investor and regulator (biotechnology). In a society that prides itself upon entrepreneurship and the ascendant power of the private sector, just how important is the public sector to the vital decisions of knowledge-intensive firms, particularly with regards to where they choose to locate? This is a critical question because of the increasingly central role that knowledge-intensive industries play in the economic development of communities and the tremendous competition for such business.

Biotechnology is a particularly salient example as the astounding rate of growth in this industry and a general desire to partake of its lucrative economic bounty has led national and regional governments to focus on the development of biotechnology clusters as a catalyst for regional economic development. Indeed, a 2002 survey of 77 local and

36 state economic development agencies in the U.S. reported that 83% have listed biotechnology as one of their top two targets for industrial development.[2] For example, St. Louis, Missouri has sought to become a player in the field of agricultural biotechnology by creating a biotech cluster in the heart of its long-neglected inner-city. Outside the United States, Singapore, a country without a biotechnology industry less than a decade ago has become an emerging powerhouse in this sector in large part because of the active role that its government has played in creating an environment conducive to the development of the industry. Specifically, the Singaporean government has successfully launched Biopolis, an 18.5 hectare, $300 million science park devoted exclusively to biomedical research and development with an explicit focus on biomanufacturing that has acted as a powerful inducement, along with an attractive regulatory regime and tax incentives, to induce global biotechnology firms to relocate to Singapore. In view of the seeming conflict between conventional wisdom dominant in the United States and government-led initiatives in countries such as Singapore, this dissertation will attempt to analyze the locational dynamics of a particular high-tech industry—biotechnology—so as to ascertain the role that government initiatives—fiscal policy; infrastructure development; and regulations play in the locational decisions of biotechnology firms in the Cambridge metropolitan area.

[2] Cortright, Joseph and Mayer, Heike. Signs of Life: The Growth of Biotechnology Centers in the U.S. The Brookings Institution Center on Urban and Metropolitan Policy, (2002), p.6.

Central Research Question

The focus of this dissertation is on the locational dynamics of a particular high-technology industry—biotechnology—during the 1990-2005 period. At present, the most important and the fastest growing segment of the emergent knowledge economy is the biotechnology industry, which involves the application of genetic engineering to specific domains ranging from food to the environment to health. The branch of biotechnology that is focused on health applications is known as biopharmaceuticals. This dissertation will focus on this area as it is by far the largest in scope. It will also use the terms biotechnology and biopharmaceuticals interchangeably. It is important to note that while it is possible to define the biotechnology sector in terms of the small, entrepreneurial firms that since the 1976 founding of Genentech, the world's first biotech firm, have focused on commercializing this emerging science, the techniques of biotechnology are utilized by a wide variety of firms including both startups and large pharmaceuticals. As a consequence, this study utilizes the term biotechnology industry to encompass both small dedicated biotech firms and large, global biopharmaceutical corporations.

While scientific knowledge as a whole has been increasing at rapid pace in general, the advances in biotechnology have been even more rapid than that of other scientific disciplines. The result has been enormous technological progress in biotechnology-related fields ranging from bioinformatics to biopharmaceuticals. This biotechnology-driven progress was reflected in the dramatic race to map the human genome and in the many new drugs that are influencing mankind's quality of life. Given the importance and dynamism of this industry, the core question is: Does the government play any meaningful role in the locational decisions of biotechnology?

Hypothesis

This dissertation is an examination of the role of government in the locational decisions of biotechnology firms in the City of Cambridge, Massachusetts, one the largest and most significant biotechnology agglomerations in the world. The historical dynamics of the biotechnology industry as well as the specific policy dynamics that have influenced development will be evaluated. The central hypothesis of this dissertation is that the success of Cambridge in attracting biotechnology firms is the outcome of a distinct set of local, state and federal government policy choices that have catalyzed the development of the biopharmaceutical industry. Each of the stakeholders in the Cambridge biotechnology community ranging from private firms to local government to the talent and scientific infrastructure offered by the City's noted academic institutions—MIT and Harvard—can make a valid claim to be the critical catalyst to the growth and development of the biotechnology cluster therein. My objective is to isolate which factor or combination of factors has been most central to the biotechnology industry in Cambridge.

Definitions

In this study, the central issue is the role of public policy in the locational decisions of a specific industry, namely biotechnology. The hypothesis will be tested through interviews of the relevant stakeholders; in depth case studies--using interviews and surveys--of the locational decisions of several firms and their employees; and an analysis of the degree to which growth and decline in the number of firms correlates with specific government policy decisions and expenditures.

Public policy as defined here refers to the actions taken by governmental authorities at the local, state and federal levels in 5 specific areas:

1) Sectoral: Policies such as the Orphan Drug Act targeted specifically at the biotechnology industry to influence the locational decisions of firms in this industry sector.
2) Physical/Zoning/Infrastructure: Policies to shape the physical environment to make it easier for firms considering settling in the area. This refers especially to the permitting process and access to critical resources such as water.
3) Fiscal: Tax policies that influence the bottom line for firms seeking to locate.
4) Human Resource Development: Policies such as federally-funded BioCareer labs that support the development of the human capital that is critical to knowledge-intensive firms.
5) Information Dissemination/Collaboration/Networking: Efforts by government to develop social capital through enhanced coordination with stakeholder groups. For example, meeting with businesses to assess their needs and putting them in contact with other community entities that can address their concerns.

The biotechnology industry is not really a distinct industry at all but rather a collection of techniques, the most important of which is genetic engineering.[3] Generally, the term biotechnology refers to a broad generic technology that is used in a wide range of industrial fields, such as food, healthcare, agriculture, and the environment to develop

[3]Feldman, Maryann. "The Locational Dynamics of the U.S. Biotechnology Industry: Knowledge Externalities and the Anchor Hypothesis." Prepared for the Dutch interuniversity research group *Technology and Economic Growth* conference on August 26-27, 2002, p.1 and "The Genetic Alternative: A Survey of Biotechnology." *The Economist*, April 30, 1988, p.10.

new products and services.[4] Biotechnology blurs many of the distinctions between the health, food, chemicals, and agricultural industries, uniting them by means of a common group of techniques.[5] However, at present, the largest category of biotechnology applications is in health and medicine: the diagnosis, treatment, and prevention of disease.[6] According to estimates by Standard and Poors, human diagnostics (15%) and therapeutics (80%)—both of which are directly related to the health care field—account for 95% of biotechnology revenues in the United States, the largest and most advanced biotechnology market.[7] Thus the overwhelming majority of the impact of biotechnology is in the health care field. The biopharmaceutical industry is closely related to the health care field in that it involves the use of biotechnology in the creation of drugs to address illness and improve quality of life.

Therapeutics which will be known as *biopharmaceuticals* in this study involves the use of biotechnology in the creation of drugs to address illness and improve quality of life. This definition is important because it is both broader and more specific. It is broader in that biopharmaceuticals has a direct relationship to the health care economy which facilitates the measurement of regional economic development impacts. It is also more specific in that it refers to a particular industry in which the techniques of biotechnology are being applied.

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[4] Van Geenhuizen, Marina. "How Small Biotechnology Firms Survive in the Dutch Pharmaceutical Industry: An Exploratory Analysis" in New Technology-Based Firms in the 1990s, vol. 6, (Pergamon: 1999), p.200.

[5] "The Genetic Alternative: A Survey of Biotechnology." *The Economist*, April 30, 1988, p.18.

[6] Cortright, Joseph and Mayer, Heike. *Signs of Life: The Growth of Biotechnology Centers in the U.S.* The Brookings Institution Center on Urban and Metropolitan Policy, (2002), p.6.

[7] Ibid.

Methodology

Specifically, pharmaceutical and medical manufacturing data in the U.S. have been collected using North American Industry Classification System (NAICS) code 3254. This includes the following:

325411 Medicinal and Botanical Manufacturing
325412 Pharmaceutical Preparation Manufacturing
325413 In-Vitro Diagnostic Substance Manufacturing
325414 Other Biological Product Manufacturing

Generally speaking the development of a cluster—a geographic agglomeration of competitiveness businesses—can best be measured by a combination of official statistical data sets, survey work, and a qualitative understanding derived from interviews with cluster members.[8] Special attention will be paid to the role of public policy in the development of the biopharmaceutical industry in the Cambridge milieu. What has been the impact of public policy in this specific context? I am specifically interested in the locational impact—positive or negative—of governmental policies in three areas: infrastructure spending, regulation, and fiscal policy.

Qualitative Analysis: To address the central questions, surveys and interviews of biotechnology cluster stakeholders in government, academia, and business will be conducted. These surveys employ open-ended questions and will focus on the myriad member organizations of the national and regional biotechnology industry associations. Since these organizations have a vested interest in identifying solutions to regional

[8] A Practical Guide to Cluster Development. A Report to the UK Department of Trade and Industry and the English Regional Development Agencies by Ecotec Research and Consulting, 2003.

problems, they are much more willing to become actively engaged in the interviewing process.

A set of actor-based questions[9] will be asked of both the primary and secondary case literature, and form the basis of the open-ended individual interviews with selected leaders of and key individuals within the aforementioned organizations. The attempt is to both elicit factual information about the case and to identify the larger role and influence of government on the locational decisions of biotechnology firms in Cambridge, Massachusetts.

Organization

Having laid the aforementioned foundation, this dissertation will proceed to outline a theoretical overview of the dynamics of the knowledge economy of which biotechnology is a part. The author will then delineate the evolution of the biotechnology industry in the United States and outline the industry as it exists in Cambridge, Massachusetts. The role of federal, state, and local governmental policies, respectively, in the locational decisions of the biotechnology firms in Cambridge will then be examined. Finally, the accumulated data and insights will be examined to assess the validity of the author's hypothesis in a formal conclusion.

[9] See Appendix.

Part II: The Knowledge Economy

To analyze how government influences the development of an industry and the locational decisions of the firms within that industry, one must first characterize the specific economic era and development context from which that industry has emerged. Biotechnology exemplifies what has been heralded as the Knowledge Economy in that human knowledge and scientific innovation are the catalyzing inputs that drive the economy. In this section, I will analyze the dynamics of the Knowledge Economy, explain how it differs from previous economic eras, delineate the new role of knowledge and innovation, and analyze its implications vis a vis urban form.

During the last three centuries, the critical drivers of wealth accumulation have shifted from natural resource endowments (resource economy); to tangible created assets such as buildings, machinery and equipment (asset economy); to the most intangible created asset, namely knowledge itself (knowledge economy).[10] This shift has profound implications for any area that must now confront a deficit of both financial and human capital. Resource economies are exemplified by countries like South Africa and Saudi Arabia, where the extraction of a natural commodity—gold and oil respectively—for which there is economic demand—drives economic growth. Struggles for control over the critical natural resource can lead to wars and authoritarian regimes which has often been the case in developing countries that have resource endowments. Asset economies use the industrial machinery in factories to transform resource inputs such as cotton or gold into finished products. China, which has become a global workshop for myriad

[10] Dunning, John, ed. Regions, Globalization and the Knowledge-Based Economy. (Oxford University Press: New York, 2000), p.8.

multinationals, is an asset economy. In an asset economy, workers are often low and semi-skilled so that the primary value that they add is not through their intellectual output but rather through the contributions of their physical labor. The factory assets are often owned by an investor class that pays workers a salary.

A Knowledge Economy is one in which knowledge is used to produce economic benefits. Nowadays, knowledge refers not only to research and development in the natural sciences and engineering, but also to related scientific activities such as surveys, statistics, mapping, etc. as well as a full range of technical, financial, managerial, and social skills and cultural contexts.[11] These are the skills that are of paramount significance to a trained workforce—students need to know that they need to know these disciplines to have any hope of making a good living. In the Knowledge Economy, math and science, which serve as the fundamental underpinnings of new economic knowledge or innovation are of paramount importance to the creation of wealth. There are three types of new economic knowledge: industry R&D; university R&D; and skilled labor.[12] Innovation is important because of the pace of technological advancement in our current society: the total amount of scientific knowledge doubles every ten years as a whole and every five years in the life sciences field. This knowledge and innovative capacity, which usually requires many years of training, is by definition scarce. Thus knowledge workers have greater bargaining authority than in previous eras as the critical asset—intellect—can leave the corporate entity at any time unless it is appropriately compensated with

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[11] Cooke, Philip and Piccaluga, Andrea, eds. Regional economies as knowledge laboratories. (Edward Elgar: Northampton, MA, 2004), p.xxii.

[12] David Audretsch and Maryann Feldman. "The Telecommunications Revolution and the Geography of Innovation" in James Wheeler, Yuko Aoyama, and Barney Warf, (eds.) 2000. Cities in the Telecommunications Age, (NY: Routledge), p.187.

sufficient financial remuneration and/or a high quality of life. Software, biotechnology, and academia are exemplars of the knowledge economy.

The United States has been a resource, asset, and knowledge economy during various phases of its history. Prior to the late 19th century, the United States was a resource economy as its wealth was a function of its being the world's leading producer of cotton. Following the end of the Civil War, the United States leveraged its natural resource rents to become an asset economy as it industrialized. Since the late 1960s, as more and more industrial production has shifted to developing countries such as China, and high-technology industries have arisen, the United States has evolved into more and more of a knowledge economy. It should be noted that economies—including the United States—are often characterized by elements of all three eras.

The Knowledge Economy has in many respects been influenced by the advent of information and communications technologies that have dramatically telescoped distances across the globe—leading some theorists such as Frances Cairncross to herald the "death of distance" and the obsolescence of central cities. Nonetheless, as is evidenced by the propensity of particular industries to concentrate heavily in specific localities, place still matters immensely in the Knowledge Economy. As Saskia Sassen has noted, the global flows of capital intrinsic to globalization has also produced "global cities" that serve as strategic bases for the financial institutions, business service firms, and high-technology start-ups which dominate capitalism in the 21st century. Cambridge, Massachusetts, a global biotechnology center that is the subject of this study, is one such example of the importance of place in the Knowledge Economy.

Technological Change and Urban Change

It is important to note that while place is important, since places are shaped by the people who live in them, the key to the dynamic between technological change and urban change is whether people have access to the educational opportunities that enable them to be empowered by technology. In the Knowledge Economy, the great divide is not spatial but rather educational. The perverse irony of our age is that many of the people who live in close proximity to the professional and scientific clusters in areas such as midtown Manhattan or Cambridge, Massachusetts are light years away from the modern economy while those who commute to downtown from the suburbs are an integral part of it. As Peter Hall has noted, "increasingly, the central economy is fed from the elite corridors and the exurbs; the ancillary workers are found in parts of the intervening areas, while other areas become in effect separate islands, no longer functionally connected with the city."[13] What the people who now live in the suburbs have is the education that has enabled them to weather the storm facilitated by telecommunications. That storm is known as globalization. Far from eliminating differences between places, the use of information and communications technology has permitted the exploitation of differences between areas, particularly in terms of local labor market conditions, the nature of cultural facilities and institutional structures.[14]

One great difference is labor cost. The globalization of production has meant that if a worker in a developing country can do "grunt" work cheaper than one in a developed

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[13] Peter Hall. "Changing Geographies: Technology and Income," in Donald A. Schon, Bish Sanyal, and William J. Mitchell, eds. High Technology and Low-Income Communities: Prospects for the Positive Use of Advanced Information Technology. (Cambridge, MA: MIT Press).

[14] J. Goddard. 1992. "New Technology and the Geography of the UK Information Economy" in Understanding Information Business, Technology and Geography, edited by K. Robbins, pp. 178-201. (London: Belhaven).

country then they will be allowed the opportunity to do so provided they possess the requisite linguistic and cultural assets. That is why call centers have been set up in Ireland and why software firms in Silicon Valley have a closer relationship with cheap software engineers in Bangalore, India than they do with their surrounding communities. Facilitated by telecommunications, a bifurcation has developed within American cities as the elite, highly-trained workers do the value-added work and the jobs that remain are essentially low-level service jobs since most of the manufacturing jobs that used to employ working class males have migrated to China and Southeast Asia and other reservoirs of cheap labor. The result has been de facto segregation as there is little incentive for business to fret over the fate of the inner-city workforce since their educational inadequacies have—until recently—had little real impact on the pool of labor available to corporate America.

The aforementioned dualistic spatial arrangement is what Manuel Castells has referred to as the dual city within the "informational city." As defined by Castells, the informational city is an urban system with socio-spatial structure and dynamics determined by a reliance of wealth, power, and culture, on knowledge and information processing in global networks, managed and organized through intensive use of information/communication technologies; and the dual city is an urban system socially and spatially polarized between high value-making groups and functions on the one hand and devalued social groups and downgraded spaces on the other hand.[15] This polarization induces increasing integration of the social and spatial core of the urban system, at the same time that it fragments devalued spaces and groups, and threatens them with social

[15] Manuel Castells. "The Informational City is a Dual City: Can It Be Reversed?" in Donald A. Schon, Bish Sanyal, and William J. Mitchell, eds. High Technology and Low-Income Communities: Prospects for the Positive Use of Advanced Information Technology. (Cambridge, MA: MIT Press).

irrelevance.[16] Even as policymakers seek to develop knowledge-intensive enterprises, they must remain cognizant of the fact that their challenge is also to find ways to overcome that polarization in the midst of challenging global forces.

It is also surprisingly apparent that new patterns of control, coordination, and dominance are being created that enable different places within cities to play a key role in how human beings live their daily lives. Rather than dying out, new patterns of development are evident both within cities and between them. Despite the alleged "death of distance," places still matter immensely in the world economy. Since location matters, identifying the factors that drive locational decisions is even more important than ever.

While the city is not becoming obsolete, its pattern of development is changing in that it is both centralizing and decentralizing. According to Peter Hall, as of the early 1990s, in the information-intensive service industries of Europe, London has 93% of the headquarters of service companies in the United Kingdom, Paris 70% of those in France, Rome 67% of those in Italy, and Frankfurt 53% of those in Germany.[17] In the United States, the financial sector has seen a similar consolidation as investment banking firms in San Francisco and Los Angeles have been bought out by East Coast rivals and New York has emerged as the clear market leader. New York like London and Tokyo benefits from being a key financial center and the hubbing of telecommunications networks has tended to reinforce its position. The same trend towards consolidation is true for the biotechnology industry where, in the United States, 9 metropolitan areas dominate the biotech sector and is increasingly evident on a regional scale as two regions—the

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[16] John Mollenkopf and Manuel Castells, eds. 1991. Dual City: Restructuring New York. (New York: Russell Sage Foundation).

[17] Peter Hall, "Moving Information: A Talk of Four Technologies," Working Paper 515, College of Environmental Design, Berkeley, 1991, p.24.

Northeast Corridor and the San Francisco Bay Area dominate the industry. Within the Northeast Corridor, the largest agglomeration of biotechnology activity is Cambridge, Massachusetts. This trend towards concentration has profound consequences for the character of economic development as the sectors of the economy performing global roles dominate the economic base of the affected areas. In turn, these agglomerations produce similar occupational and earnings hierarchies resulting in similar social outcomes.

The character of the labor markets that emerge under the urban agglomerations created by the Knowledge Economy have profound implications for society and hence for public policy. In Sassen's view, the particular industrial and occupational economic structure of the global city region leads to social polarization and a bifurcated earnings structure due to the prevalence of industries that hire a disproportionate number of high and low wage workers and that in turn creates the outcome of the "disappearing middle."[18] As Danziger and Reed elegantly summarize:

> "*Labor-saving technological changes have simultaneously increased the demand for skilled workers* who can run sophisticated equipment and reduced the demand for less-skilled workers, many of whom have been displaced by automation. *Global competition has increased worldwide demand for the goods and services produced by skilled workers in high-tech industries* and financial services. Lower-skilled workers increasingly compete with low-wage production workers in developing countries. Immigration has increased the size of the low-wage workforce and competition for low-skilled jobs. Institutional changes, such as the decline in the real value of the minimum wage and shrinking unionization rates, also moved the economy in the direction of higher earnings inequality.[19]

[18] Sassen, S. (1991). The Global City: New York, London, Tokyo. Princeton, New Jersey. Princeton University Press.

[19] Danziger, S. and Reed, D. (1999) "Winners and Losers: The era of inequality continues" in *Brookings Review*, Fall 15-17.

Given the central role of locational analysis in this study, this point about the continued relevance of cities bears emphasis. The continued importance of urban location—as opposed to the death of distance due to the impact of telecommunications—is reinforced by Blair Badcock, who argues that there are four major factors that have contributed to both the growing relevance of urban agglomerations and changes in the productive capacity of cities in the late 20th century.[20] These include:

- Resource-based primary production accounts for a diminishing share of export income and job creation relative to *expanding, city-based sectors of the economy* like elaborately transformed manufactures (ETMs), producer services, educational exports and tourism
- Within the industrial sector of the knowledge economy, production is becoming less energy- and labor-intensive, and more dependent on expert systems and the processing of information. *Large cities provide a stimulating and synergistic intellectual milieu, where institutions of higher learning and R&D labs cluster, and innovative ideas in media and fashion are exchanged.*
- *Because of the high degree of interaction between firms using flexible systems in production, including the sharing of orders, facilities, technical information and machine tools, and marketing and trade services, it is not uncommon to find them clustering in cities*—though outside the traditional industrial districts with their organized labor and congestion costs.
- Profits generated from international trade in commodities, finance and business services and technology are replacing productive activity per se as the driving force in the global economy. *As a result, a few select cities have acquired an unrivaled economic and strategic influence over capital flows and local of new investment around the world. [My emphasis]*

The cores of the aforementioned major cities all employ highly trained knowledge workers in industries that now constitute the key urban economic drivers: finance and business services, command and control functions for international companies and agencies, creative and cultural industries, the media and design professionals.[21] If the

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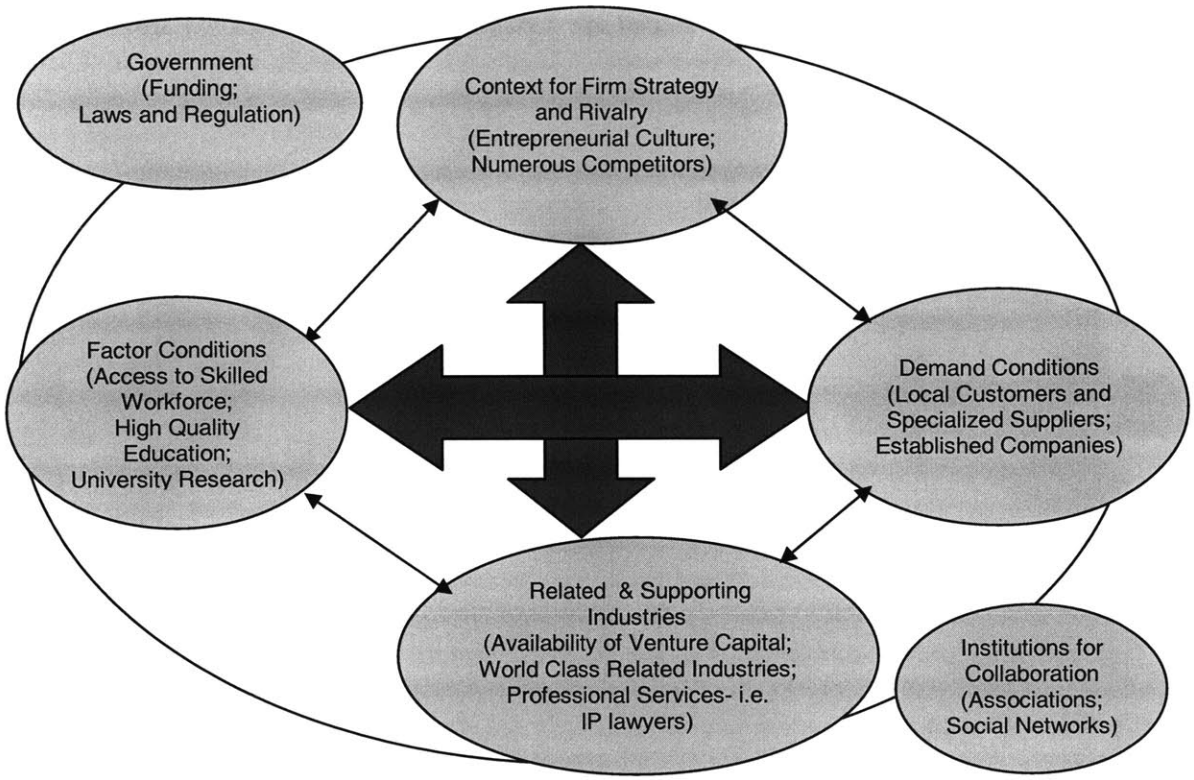
[20] Badcock, Blair. Making Sense of Cities: A Geographical Survey. (London, 2002: Arnold Publishers), p.65.

[21] Peter Hall. "Changing Geographies: Technology and Income," in Donald A. Schon, Bish Sanyal, and William J. Mitchell, eds. High Technology and Low-Income Communities: Prospects for the Positive Use of Advanced Information Technology. 1998, (Cambridge, MA: MIT Press).

phenomenon of dominant cities is expanding to be evidenced in the dominance of particular regions, then a question arises as to whether the deleterious socio-economic development impacts described by Sassen are also expanding accordingly. Part of the challenge is to understand the competitive advantages of cities and empower local residents to leverage those advantages to create wealth and complement low employment but high revenue knowledge industries such as life sciences.

So in the Knowledge Economy, place still matters in that human capital must still co-locate in workplaces in firms rooted in urban locales so as to maximize production. The firms often organize into geographic concentrations of business known as clusters. Michael Porter, the most famous proponent of the industrial cluster concept, defines clusters as geographic concentrations of interconnected companies, specialized suppliers, service providers, and associated institutions in a particular field that are present in a nation or region:[22]

[22]Porter, Michael. "Location, Clusters, and Company Strategy" in Gordon Clark, Maryann Feldman and Meric Gertler, (eds.) 2001. The Oxford Handbook of Economic Geography, (Oxford, England: Oxford University Press) pp.258-9.



Diamond Model of a Cluster[23]

Porter argues that traditionally, attempts to explain concentrations of firms in terms of agglomeration economies stress cost minimization due to proximity to inputs or proximity to markets but these explanations have been undercut by the globalization of markets, technology, and supply sources, increased mobility, and lower transportation and communications costs.[24] In the author's view, these clusters are characterized as follows:

1) Strong pre-commercial R&D capabilities—Defense, National Institutes of Health funding, etc.
2) Ongoing private sector investment—i.e. venture capital
3) World class universities as sources of scientific personnel, equipment, and knowledge spillover
4) Social Capital: Networking fostered by proximity to major institutions of

[23] Based upon the diamond model as articulated by Michael Porter in On Competition, 1998.
[24] Ibid.

> higher learning is critical high-tech clusters tends to thrive when customers, talent pools, and thought leaders consistently interact

Clusters are especially important as studies by Audretsch and Feldman suggest that knowledge spillovers tend to be geographically bounded within the region where the new economic knowledge was created, which is to say that innovation may spill over, but the geographic extent of such knowledge spillovers is limited.[25]

Within high-tech clusters the most important input is new economic knowledge or innovation. In previous clusters such as the industrial districts studied by Alfred Marshall in The Principles of Economics, worker proximity to a heavy industry such as steel, ship building, etc. helped place them in position to add value with their physical labor. Such proximity also promoted innovation by facilitating the interaction and knowledge exchanges that are critical to the creation of new knowledge. But in a high-tech cluster, workers must not only live in proximity but must also be possessed of a high level of education. In that sense, innovation according to Marshall is more of a bottom up phenomenon while in a high-tech industry like biotechnology it is more of an elite process.

Innovation is important because of the pace of technological advancement in our current society. As Beat Hotz-Hart has noted: "Competitiveness is becoming more dependent upon the ability to apply new knowledge and technology in products and production processes. But, with the rapid advancement of knowledge, firms are forced into an active search process. For complementary knowledge and know-how, firms increasingly rely on interaction with a variety of actors."[26] This means that locales—both

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[25]David Audretsch and Maryann Feldman. 1996. "R&D Spillovers and the Geography of Innovation and Production." *The American Economic Review*, vol. 86, no. 3, pp.634-5.
[26]Beat Hotz-Hart. "Innovation Networks, Regions, and Globalization" in Gordon Clark, Maryann

metropolitan and regional—and clusters where that *interaction* can productively occur are of paramount importance. As outlined by Beat Hotz-Hart, there are 5 success factors for the functioning of innovation processes within a cluster[27]:

- Better access of firms to information, knowledge, skills and experiences
- More intense linkages and co-operation
- Higher response capacity
- Reduction of risks, moral hazard, information and transaction costs
- Better trust base and social cohesion

Social capital—a residual or side effect of social interactions and an enabler of future interactions[28]--is key to all of these success factors because there is a lot of informal, tacit professional knowledge that is transmitted through social and commercial relationships and informal cooperation.[29] In these "milieux of innovation," there are specific sets of social relationships of production and management, based upon common instrumental goals, sharing a work culture, and generating a high level of organizational synergy.[30] That is why industrial clusters like Silicon Valley remain so vital. In a human society, face to face contact and discussions over lunch or on the golf course still have a great deal of relevance.

Innovation, the hallmark of high-tech clusters, does not arise in isolation but rather is an interactive social process. The tacit nature of knowledge and the social nature of the innovation process makes the social interaction within clusters of critical

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Feldman and Meric Gertler, (eds.) 2001. The Oxford Handbook of Economic Geography, (Oxford, England: Oxford University Press), p.433.

[27]Ibid, p.434.

[28]Paul Resnick. 2002. "Beyond Bowling Together: SocioTechnical Capital" in John M. Carroll (ed.), Human-Computer Interaction in the New Millenium, (NY: ACM Press), p.648.

[29]AnnaLee Saxenian. "Regional Networks and the Resurgence of Silicon Valley."California Management Review, vol. 33, no. 1, Fall 1990, p.105.

[30] Manuel Castells.1989. The Informational City: Information Technology, Economic Restructuring and the Urban-Regional Process. (Cambridge, MA: Basil Blackwell, Inc.), p.72.

importance.[31] The complexity of the knowledge in high-tech disciplines and the fact that it is highly tacit in nature, makes face-to-face interaction and communication through geographic proximity important to its transmission as the less codified and the more difficult it is articulate the knowledge, the greater the need for frequent face-to-face meetings and the greater the resulting degree of centralization in geographic agglomerations.[32] This idea is further espoused by Edward Leamer and Michael Storper who argue that the economy is increasingly dependent on the transmission of complex uncodifiable messages, which require *understanding and trust* that historically have come from face-to-face contact.[33] This is not likely to be affected by information technologies, which allows long distance "conversations" but not "handshakes".[34] Being co-present in clusters allows for learning through networking and interaction and this is a critical factor driving agglomeration into high-tech clusters. As Breschi has noted:

> [A] key feature of successful high-technology clusters is related to the high level of embeddedness of local firms in a very thick network of knowledge sharing, which is supported by close social interactions and by institutions building trust and encouraging informal relations among actors. This is the...crucial issue that is, almost invariably, associated with well-developed and effectively functioning technology-based clusters. The possibility for individual firms to tap into the body of localized knowledge and capability depends, in a fundamental way, on the ability to establish and maintain effective social links and lines of communication.[35]

These innovation-producing interactions in high-tech clusters are facilitated by social capital. They suggest that productive resources can reside not just in things and in people but also in social relations among people as networks of people who have developed

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[31] Maryann Feldman. 2002. "The Internet Revolution and the Geography of Innovation." *International Social Science Journa*l. 54: 47 – 56.
[32] Ibid.
[33] Edward Leamer and Michael Storper, 2001. "The Economic Geography of the Internet Age." NBER Working Paper No. 8450. (Cambridge, MA: National Bureau of Economic Research), p.1.
[34] Ibid.
[35] Stefano Breschi and Franco Malerba. 2001. "The Geographic of Innovation and Economic Clustering: Some Introductory Notes." *Industrial and Corporate Change*, vol. 10, no.4, pp.819-20.

communication patterns and trust can accomplish much more than a bunch of strangers, even if the two sets of people have similar human, physical, and financial capital available.[36] Social capital can facilitate information routing and enable the coordination of interdependent actions but most importantly it produces the trust that is critical to risk-taking in resource exchange.[37] All of this promotes innovation. In Regional Advantage: Culture and Competition in Silicon Valley and Route 128, Annalee Saxenian's comparison of the underlying cultures that influenced the success of these two high-tech clusters, she argues that the difference between the two regions was social capital in that Silicon Valley's dense social networks and open labor markets encouraged experimentation and entrepreneurship.[38] The imperative of social interaction to support innovation puts a premium on geographical clustering, especially in the biotechnology industry.

Conclusion

Thus, in the Knowledge Economy in which the biotechnology industry is rooted, place is an economic context in which intellectual capital and innovation as opposed to natural resources or industrial assets are critical to success. Despite the advent of distance telescoping technologies such as telecommunications, the Knowledge Economy remains one in which firms still find it advantageous to network through business clusters situated in dominant urban agglomerations such as Cambridge, Massachusetts. Those agglomerations place a premium on highly skilled talent and discount the value of the low and semi-skilled which has public policy implications for how to deal with those

[36] Ibid, p.647.
[37] Ibid, pp.652-655.
[38] Annalee Saxenian. 1994. Regional Advantage. (Cambridge, MA: Harvard University Press), p.2.

whose skills are least demanded by the Knowledge Economy. Most importantly, this chapter demonstrates the critical importance that the firms, who are key actors in the Knowledge Economy, must attach to being situated in the appropriate milieu because it is such a critical component of competitive advantage.

Part III: Biotechnology and Regional Innovation

Having established the importance of locational decisions for knowledge-intensive firms in the Knowledge Economy, a deeper exploration of the dynamics of the geographic context in which those locations are situated is required. As shall be later demonstrated, the Cambridge metropolitan area increasingly functions along with other geographical agglomerations so it is important to provide a theoretical framework for understanding that process. The argument herein is that in the current economic context, increasingly regions--whether they be broader regions such as the Northeast Corridor or metropolitan regions such as the Boston/Cambridge area--are the central units of economic activity. The Boston/Cambridge metropolitan area is a critical node in the broader Northeast Corridor region which is the largest biopharmaceutical agglomeration and production system in the world. It plays a distinct role as a center for university R&D—much of which is publicly funded—and a major agglomeration of biotechnology startups. According to Michael Storper: "Increasingly, it is recognized that the engines of national economic performance are subnational technology districts that are characterized by strong ties between regional actors."[39] More and more, cities that are networking with other cities and regions—not just single municipalities—are emerging as critical players in the Knowledge Economy. Silicon Valley, a famous bastion of innovation in information and communications technologies, is one such network. Cambridge, which is a critical component of the global biotechnology industry is another node in a broader network. The Northeast Corridor with its host of educational institutions and robust life

[39] Storper, Michael. (1995) The resurgence of regional economics, ten years later: the region as a nexus of untraded interdependencies, *European. Urban & Regional. Studies* 2, pp.191-221.

sciences industry is another such network. This trend of city-to-city networks is due to the association between organizational and technological learning that takes place within regional agglomerations. There are two dimensions to this association. Firstly, there are *traded interdependencies* that constitute webs of user-producer relations essential to information exchange.[40] Secondly, there are *untraded interdependencies* such as labor markets, norms, values and public or quasi-public institutions that become intrinsic to the process of continuous learning and innovation that is so essential in the Knowledge Economy.[41] As Michael Storper has noted: "Where these input-output relations or untraded interdependencies are localized, and this is quite frequent in cases of technological or organizational dynamism, then we can say that the *region is a key, necessary element in the `supply architecture' for learning and innovation.*"[42] This trend towards regional interdependence or networking has been characterized as a *regional innovation system* by Michael Fritsch and the Northeast Corridor is one such system. A regional focus on innovation is regarded as especially appropriate when maintaining roots in a particular cluster is important to a firm but the benefits derived from short-distance interaction with other clusters plays a significant role in the competitiveness of the firm.[43] For example, the biotechnology startups in the Boston area have significant interaction with the large pharmaceutical firms in the New York-New Jersey metropolitan area.

Fritsch identifies the components of a regional innovation system: institutions for research, education, and other forms of knowledge transfer; manufacturing

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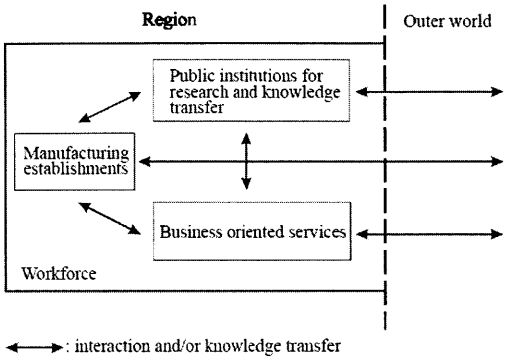
[40] Morgan, Kevin. "The Learning Region: Institutions, Innovation and Regional Renewal," *Regional Studies*, 1997, vol. 31, number 5, p.495.

[41] Ibid.

[42] Storper, Michael. (1995) The resurgence of regional economics, ten years later: the region as a nexus of untraded interdependencies, *European. Urban & Regional. Studies* 2, pp.191-221.

[43] Fritsch, Michael. "Do Regional Systems of Innovation Matter? Freiberg Working Papers, Technical University Bergakademie Freiberg-Faculty of Economics, N.3, 2003, p.7.

establishments or firms; the suppliers of business-oriented services; and a regional workforce:[44]



Model of a Regional Innovation System[45]

Research institutions generate, accumulate, and distribute information—particularly at the pre-commercial level in the pure sciences. They then transfer that information to entrepreneurs and start-ups through licensing arrangements. The regional workforce serves as a source of both highly skilled labor to staff the components of the regional innovation system and as a pool from which entrepreneurs arise who commercialize the innovations of the major research institutions. They are supported in these efforts by business-oriented service personnel such as intellectual property lawyers and venture capitalists. Manufacturing establishments act as final producers and serve to provide marketing expertise and distribution channels for the innovations of the entrepreneurs. The regional dimension of these activities is of considerable relevance for new firm formation processes because most founders of new businesses are regionally embedded

[44] Ibid.
[45] Ibid.

and come from firms and research institutions in the same region in which they start their businesses.[46]

In many respects, a regional innovation system is comparable to what Cooke has referred to as a "megacenter." Megacenters are science-driven, public and privately funded institutional complexes that in the case of the biopharmaceutical industry have as their ultimate goal the production of patient healthcare.[47] They are hierarchical networks that include industrial hierarchy expressed in the ever-concentrating ownership structure of big pharmaceutical firms, government hierarchy regarding basic research funding and regulation of bioscience, and research hierarchy, in that most of it is concentrated in medical schools, hospitals, and universities.[48]

Like the regional innovation system concept, megacenters are concerned with capturing the knowledge value chain from exploration, through examination to exploitation of knowledge.[49] Cooke argues that in contrast the cluster concept as articulated by Porter is fundamentally concerned with proximate business interactions for competitiveness and commercialization of innovation, and hence with markets alone. However, Cooke fails to note that Porter's concept of the cluster has evolved to increasingly account for the role of government, especially in his examination of health care and high-technology industries which rely upon pre-commercial federal research and development. Secondly, the argument herein is that the regional innovation system concept does not invalidate the cluster concept as it allows clusters—each with a

[46] Johnson, P.S. and Cathcart, D.G. (1979): New Manufacturing Firms and Regional Development: Some Evidence from the Northern Region, *Regional Studies*, 13, pp.269-280.
[47] Cooke, Philip. "The molecular biology revolution and the rise of bioscience megacentres in North America and Europe." Environment and Planning C: Government and Policy, 2004, vol. 22, pp.161-77.
[48] Ibid.
[49] Ibid.

particular comparative advantage—to be linked together for mutual benefit across a region. Nonetheless, a regional innovation system is particularly useful as a way of thinking about the biopharmaceutical industry because the increasing cost of research and development and the imperative of developing competency in new biological scientific techniques outside the immediate skill set of large pharmaceutical firms have necessitated networking and collaboration with small entrepreneurial biotechnology firms. While hierarchy remains—the small firms are dependent upon the large firms for commercialization and market access—the specialized nodes in the process of innovation have become horizontal as is exemplified by how the value chain has been organized horizontally across regions instead of vertically within single firms. This trend towards specialization within the biotechnology industry's regional innovation process will be delineated in a later discussion of the biotechnology value chain.

The increasingly essential networks within regional innovation systems are characterized by reciprocity; interdependence; power; and loose coupling. Networks exhibit reciprocity in that economic transactions occur neither through discrete exchanges (as in markets) nor by administrative fiat (as in hierarchies).[50] Instead, in networks, exchange entails indefinite, sequential transactions within the context of a general pattern of reciprocity.[51] These networks are also stable which leads to interdependent relationships.[52] Nonetheless, power also plays a role in these relationships. In the case of the biopharmaceutical industry, power is asymmetrically distributed between large pharmaceutical firms who have great distribution and marketing capabilities and the

[50] Grabher, Gernot. "Rediscovering the social in the economics of interfirm relations" in The Embedded Firm: On the Socioeconomics of Industrial Networks, ed. Gernot Grabher, (New York: 1993), pp.8-11.
[51] Ibid.
[52] Ibid.

small biotechnology firms that seek to "cash out" by being acquired or having their technology purchased. Lastly, the characteristic of loose coupling—a flexible, resilient relationship between two or more systems with some kind of exchange relationship—is particularly important. Regional networks are designed to benefit from the strength of "weak ties". This loose coupling preserves some autonomy of the exchange partners and hence prevents them from being locked into specific exchange relations. It also:

> ...affords for favorable conditions for interactive learning and innovation. Networks open access to various sources of information and thus offer a considerably broader learning interface than is the case with hierarchical firms ...*loose coupling within networks affords for favorable conditions for interactive learning and innovation. Networks open access to various sources of information and thus offer a considerably broader learning interface than is the case with hierarchical firms*...In loosely coupled systems where the identity, uniqueness, and separateness of elements is preserved, the system potentially can retain a greater number of solutions than would be the case with a tightly coupled system'[53] [my emphasis]

The importance of loose coupling is exemplified by the decline of the German Ruhr, a polycentric urban agglomeration of 5 million people, that was a center for iron and steel production.[54] This is an example of what can happen without the flexibility that loose coupling offers. During the first half of the 1980s, the Ruhr lost more than 100,000 jobs. The region's decline has been attributed to the fact that the long term stability and predictability of demand for iron and steel favored close and stable linkages between the regional core firms and the supplier sector. As a consequence, the region fell prey to the rigid specialization trap as the personal cohesiveness and well-established relations within the coal, iron and steel complex turned out to be counterproductive. When new production technologies emerged, established companies remained locked into existing technological trajectories. Rather than attempting to capitalize on the possibilities offered

[53] Ibid.
[54] Ibid.

by the emergence of a superior new substitute technology, they vigorously defended their position through the accelerated improvement of the old technology.[55] However, the argument herein is that regional innovation systems may be less susceptible to the problems of "lock-in" because the knowledge-intensive industries (unlike iron and steel) that are driving their development are primarily concerned with innovation. Consequently, loose coupling and ever-shifting alliances to combat the unpredictability of a highly competitive marketplace is essential to the actors in modern regional innovation systems.

All of this demonstrates that not only are regions in and of themselves a key factor in the innovation process but also that the character of the specific region affects the locational decisions of the firms therein. This is consistent with McKelvey's notion that environmental selection pressures—socio-economic structures that influence the behavior and performance of firms—affect the biotechnology firm's innovative search activities, and the empirical impacts are visible on (1) the existence of networks and of firms in a defined geographical locality and (2) the patterns and specializations of innovations within the population of firms in that locality.[56] Environmental selection pressures have three dimensions:

> **1) Market transactions and economic impacts**. The act of introducing innovations onto a market affects competitive pressures, and thereby the decisions of individuals, firms, and organizations.
> **2) Institutions and interactions**. Rules and routines seen through interactions among actors.

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[55] Ibid.
[56] McKelvey, Maureen. "Evolutionary economics perspectives on the regional-national-international dimensions of biotechnology innovations." *Environment and Planning C: Government and Policy*, 2004, vol. 22, pp.179-97.

3. Scientific and technical knowledge. The further development of scientific and technical (including engineering practice) knowledge affects the boundaries of search space open to the firm.[57]

This environmental selection framework facilitates an examination of the American national and regional context in which Cambridge, Massachusetts hosts a biotechnology cluster:

Regional Dimensions of Environmental Selection Process[58]

	Market Transactions and Economic Impacts
Northeast Corridor	• Strong Venture Capital Linkages • Extensive Network Connections Between Firms • Substandard broadband and wireless infrastructure • American shipping and finance center
	Institutions and Interactions
Northeast Corridor	• Extensive government funding of academic research • Strong linkages between private and academic sectors • Regional governors have significant

[57] Ibid.

[58] Template based upon the work of Maureen McKelvey, "Evolutionary economics perspectives on the regional-national-international dimensions of biotechnology innovations." *Environment and Planning C: Government and Policy*, 2004, vol. 22, pp. 179-97.

	policymaking and financial authority so greater ability to experiment—i.e. financing of stem cell research is forbidden by federal government but continues at the state level
	Knowledge, Scientific, and Technical
Northeast Corridor	• Status as global center for biotechnology R&D and human resource training • Weak kindergarten through high school educational system • High cost of health care attracts investment

A regional innovation system is also similar to what Bengtke Lundvall has described as a "learning economy". In a learning economy, communication amongst industry stakeholders is one of the major mechanisms of new knowledge creation because a significant component of the knowledge that is relevant for innovation processes is tacit—not codified—and therefore "sticks" with the respective individuals in their locale.[59] That locale may be a specific market, an institution or firm, or increasingly, a particular region. Path-dependencies and external effects such as agglomeration economies in the creation of knowledge lead to a *regional embeddedness* of innovation

[59] Fritsch, Michael. "Do Regional Systems of Innovation Matter? Freiberg Working Papers, Technical University Bergakademie Freiberg-Faculty of Economics, N.3, 2003, p.7.

activity.[60] Path-dependency refers to the view that technological change in a locality depends on its own past. History matters.

It should be noted that there are alternatives to the concept of the regional innovation system. In particular, Harald Bathelt has argued that clusters can rarely be viewed as regional systems.[61] He contends that at a geographical scale, a self-referential system is unlikely to develop because regions are strongly dependent on national institutions and other external influences and lack important political decision-making competencies. Bathelt believes that norms, accepted rules, habits, conventions and other institutional arrangements are of central importance to enable inter-firm communication and collaboration within a cluster and that this does not exist automatically.[62] Rather it is created through social practices and the establishment of institutions within a cluster that help to stabilize producer-user relations and stimulate trust.[63] While Porter contends that clusters can exist at a local, regional or even interregional and cross-national level, Bathelt argues that this is a flawed view because it does not encompass an explanation for the internal mechanisms which are responsible for the spatial relations and boundaries of the cluster. To Bathelt, the absence of a sound institutional framework makes the expectation that a precise, all-encompassing definition for clusters can be found appear unrealistic. Since institutional contexts vary between technologies and between nation states, clusters can be characterized by a different sectoral mix, complexity and spatial reach. Also, the common credentials and shared intellectual paradigm that flows from

[60] Ibid.
[61] Bathelt, H. "Geographies of production: growth regimes in spatial perspective." in *Progress in Human Geography* 29, 2 (2005), pp.204-216.
[62] Ibid.
[63] Ibid.

participation in the life sciences community tends to create a framework of shared experiences and personal contacts within regions that builds trust.

Regions are also important because globalization leads towards specialization and that reinforces national patterns of economic specialization because of regionally unequal distribution of innovation capabilities.[64] The innovative potential of regions depends on internationally immobile factors such as highly skilled labor, niche markets, research institutions or regulation.[65] This view is reinforced by Michael Porter. As Porter sees it, while the globalization of competition has indeed nullified some traditional sources of competitive advantage tied to location, such as access to raw materials, capital, or low cost labor, it has not eliminated the importance of the regional agglomerations—wherein the aforementioned immobile factors are situated—in competition.[66] Regions also matters because they facilitate the innovation that is so critical to knowledge-intensive firms, and companies must therefore broaden their approaches to the management of innovation accordingly: by developing and commercializing innovation in the most attractive location, taking active steps to access locational strengths, and proactively enhancing the environment for innovation and commercialization in locations where they operate.[67] The importance of regions for innovation is evident in the biotechnology industry in that more than 75% of all biotechnology pharmaceutical patents originate in a few regional high-tech clusters in the U.S.[68]

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[64] Beat Hotz-Hart. "Innovation Networks, Regions, and Globalization" in Gordon Clark, Maryann Feldman and Meric Gertler, (eds.) 2001. The Oxford Handbook of Economic Geography, (Oxford, England: Oxford University Press), p.445.

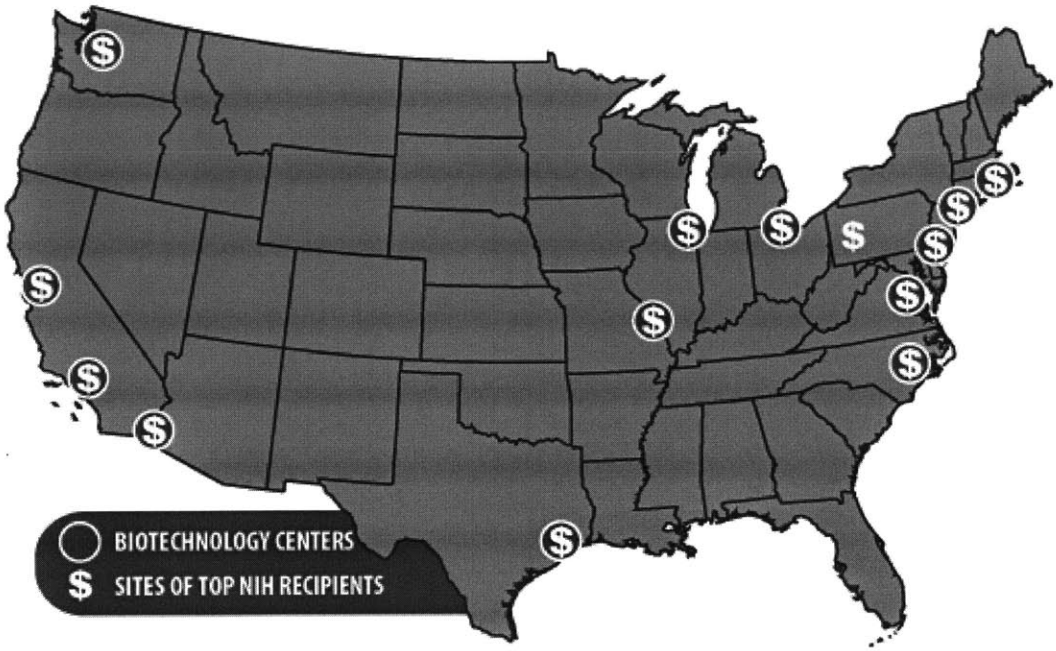
[65] Ibid.

[66] Michael Porter and Rebecca Wayland. 1995. "Global Competition and the Localization of Competitive Advantage." *Advances in Strategic Management*, vol. 11A, pp.78-9.

[67] Michael Porter and Scott Stern. 2001. "Location Matters." *MIT Sloan Management Review*, p.29.

[68] Ibid, p.35.

Biotechnology Centers in the United States[69]



Regions are also regarded as the smallest economic unit at which interrelated industries and firms can cluster in production groups of integrated suppliers. The regional clusters are important because the density of these relationships means that if the demand or supply for a particular product is not forthcoming from one firm, another will likely step up to the plate. In such an environment, individual firms feel the security necessary to expand design and/or production facilities to a size where each can achieve the lowest possible costs. Regions offer the minimum size at which markets and business networks achieve the low-cost economies of scale necessary to compete in international markets. Relatedly, regions may offer the maximum size at which working relationships can be crafted and sustained. This line of reasoning is pursued by Annalee Saxenien in

[69] http://lifesciences.iu.edu/background/research.shtml

Regional Advantage: Culture and Competition in Silicon Valley and Route 128,[70] her influential study wherein she argues that the geographic proximity of firms in a region promotes the repeated interaction and mutual trust needed to sustain collaboration. Collaboration, in turn, leads to joint efforts and the continual transmission of new technologies and innovation. This mutual trust or what Robert Putnam has termed "social capital" remains vital to economic success in spite of the spread of information technologies like e-mail and telephony. The importance of proximity and social capital within the context of a region has profound implications for the inner city because increasingly it puts a premium on the value of scarce inner city real estate—particularly for space-intensive industries like biotechnology that require lots of lab space—but it also means that the fates of distressed inner city communities are dramatically affected by their metropolitan-wide relationship with the regions of which they are a part.

The dynamic within regions has increasingly been studied by academics. Increasingly it is being argued by prominent academics such as Manuel Pastor that the schism between the city and the suburb is a false dichotomy. Rather Pastor and others contend that regions, which include both cities and suburbs, are the central unit of economic activity in modern America. In Regions That Work: How Cities and Suburbs Can Grow Together,[71] Manuel Pastor along with Peter Dreier, J. Eugene Grigsby, and Marta Lopez-Garza argue that there is a profound interdependence between cities and suburbs. This is evident as the chronic fiscal problems and deepening poverty that have plagued cities for years are increasingly evident in suburbs. The fact that these problems

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[70] Saxenian, Annalee. Regional Advantage: Culture and Competition in Silicon Valley and Route 128. (Cambridge, MA: Harvard University Press), 1994.

[71] Manuel Pastor, Peter Drier, J. Eugene Grigsby, and Marta Lopez-Garza. Regions that Work: How Cities and Suburbs: How Cities and Suburbs Can Grow Together. (Minneapolis: University of Minnesota Press), 2000.

are co-existent in both urban and suburban areas suggests that the divide between the two zones is lessening and that the two adjacent areas are morphing into a single whole. For example, the authors point out that although poverty rates are still twice as high in central cities, 30.5% of the nation's poor actually live in suburbs.[72] This is further reinforced by the fact that the 1990 poverty rates in El Monte, Rosemead, and several other San Gabriel Valley cities were about the same as in L.A. Clearly, cities and suburbs increasingly share a common destiny.[73] Yet that destiny is not just negatively correlated with shared problems. The evolution of cities and suburbs into a single economic unit is rooted in the reasons why businesses make locational decisions. As Pastor notes, businesses base their decisions not just on relative costs, but on an evaluation of the entire geographically based infrastructure of skills, markets, and expertise. These assets are what make it worthwhile for businesses to accept higher costs in return for access to skilled labor, supportive business suppliers, and the opportunity to engage in face-to-face contact with workers. Increasingly, these assets, which are critical to capitalize on economic opportunities, are constituted at the *regional level.*

Place Matters: Metropolitics for the 21st Century,[74] which was authored by Peter Dreier, John Mellenkopf and Todd Swanstrom, further reinforces the argument that the region is the central unit of economic activity. Specifically, the authors point out how the complementarity of the labor markets in the inner cities and suburbs has transformed them into a single interdependent region. Quite simply, there now exists a profound spatial mismatch of skills. The entry-level jobs with low to moderate education and skill

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[72] Ibid.
[73] Ibid.
[74] Peter Drier, John Mellenkopf and Todd Swanstrom. Place Matters: Metropolitics for the 21st Century. (Lawrence: University Press of Kansas), 2004.

requirements, such as routine manufacturing, retail, and data-entry positions, have been declining in central cities and growing on the urban fringe. Meanwhile, exclusionary zoning regulations prevent people who could take these jobs from moving nearer to them by limiting affordable housing in the suburbs. At the same time, the number of highly skilled professional jobs, such as lawyers, bankers, management consultants, etc. has increased in central business districts, but those who hold them often live in the suburbs. Since most of the job growth for lower wage jobs has actually occurred in the malls of the suburbs, the lower-income/lower educated people who do such work live in the central cities and must pay more to commute there. Likewise, the higher-income/higher-educated people who work at many of the white collar jobs in central cities live in suburbs and must endure long commute times to get to them. Because of the aforementioned imperative of face-to-face contact to promote innovation, it makes sense for companies—particularly those in information-intensive industries—to locate their most productive workers on the most expensive land and office space at the center of metropolitan areas. Given this spatial mismatch, there is a real need for both workforce development and efforts to promote asset-ownership within inner city communities so that residents can find work in or near the areas in which they live. Efforts that promote the development of an industrial base within the inner city are of paramount importance.

Just as saliently, the authors of Place Matters dispel the argument that suburbs are now replicating all the place-based functions performed by central cities in regional economies. It has been argued by authors such as Joel Garreau that "edge cities" such as Palo Alto and White Plains are becoming "mini-central cities" in the suburban realm. Therefore, since all essential economic functions can move to the suburban fringe, then

outer-ring suburbanites need not worry about the fate of cities or inner-ring suburbs. Place Matters refutes that argument by pointing out that although the urbanization of the suburbs has clearly matured—as the multiplication of suburban office complexes and shopping centers bears out—it has not come directly at the expense of central business districts, which have continued to expand. As a result, suburban property values still depend on the availability of jobs in central cities. Indeed, according to Joseph Perky, Elliot Sclar and Wim Wiewel in *Does America Need Cities? An Urban Investment Strategy for National Prosperity* in 1989, 46% of all earnings in San Francisco suburbs came from residents who worked in the central city; the figure for Denver was 41%, and 39% for New Orleans.[75] Suburban firms are not separate from the city but continue to rely on the rich supply of corporate services, such as banking, law, and accounting, found in city centers. One study of 5,000 large firms found that 92% of the professional service purchases in the region were supplied by central city firms. Alex Schwartz, the author of the study ("Subservient Suburbia: The Reliance of Large Suburban Companies on Central City Firms for Financial and Professional Services")[76] concluded that suburbia does not yet comprise an economically autonomous 'outer city' or 'edge city'.

Lastly, the authors of Place Matters provide their own perspective—which reinforces many previously stated ideas—on why businesses still continue to locate high-paying jobs in cities despite the fact that the workers live in the suburbs. The reason is density. Density nurtures economic dynamism and productivity. Specifically, employment density increases firms' productivity, regardless of workers' skills or

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[75] Joseph Persky, Elliot Sclar, and Wim Wiewel. Does America Need Cities? An Urban Investment Strategy for National Prosperity. 1991. Washington, D.C.: Economic Policy Institute.

[76] Alex Schwartz. "Subservient Suburbia: The Reliance of Large Suburban Companies on Central City Firms for Financial and Professional Services." *Journal of the American Planning Association*, June 22, 1993.

companies' capital investments. The concentration of economic functions in one area reduces the costs of transportation and exchange for the company and increases each business's access to skilled and specialized labor. Companies in the downtowns of large cities can, for example, get easy access to highly specialized, highly productive lawyers and consultants. Even if they are highly compensated, their expertise makes them worth it. As the authors of Place Matters deftly articulate, dynamic business clusters can exist in the suburbs, but cities generally foster higher levels of density and dynamism. It is difficult to imagine cutting-edge clusters in fashion, theater, art, advertising, investment banking, or design prospering in low-density suburbs. Likewise, Richard Florida argues in The Flight of the Creative Class that a sound urban policy is one that makes cities denser because urbanization economies and density are fundamental drivers of economic growth. In short, regional prosperity (and suburban well-being) still depends on good central-city performance. The development of the inner city, which is where most of the underutilized real estate in the urban core is located, will be crucial to the promotion of density. Ultimately, it makes as much sense to talk about suburban independence from the region as it does to talk about the independence of the head from the stomach. The parts of a region form an integral whole that is more than the sum of its components. These integrated metropolitan economies are the engines of American prosperity. The different parts relate to each other by specializing in different functions.

Conclusion

There are several reasons that the region has become the central unit of economic activity, especially for knowledge-intensive industries like biotechnology. Firstly, networked regions are a critical unit of development for the biotechnology industry. This is because networked regions are sufficiently well-integrated to function as a regional innovation system. As the pace of scientific change accelerates, more and more scientific organizations must reach outside of their own internal competencies to embrace the skills existent in other locales and networked—i.e. polynuclear—regions facilitate this. Secondly, reciprocal social networks that allow firms to both work together and independently so as to share costs, innovate through collaborate and benefit from specialist competencies are critical to the success of the biotechnology industry. These social networks which take root in clustered agglomerations of firms and research institutions are critical to the vitality of the biotechnology industry. As shall be demonstrated in the upcoming chapter, in no knowledge-intensive industry is this more true than in the biopharmaceutical industry which has had to transition from a scientific base rooted in chemistry base to one rooted in the ever-changing field of molecular biology.

Part IV: Biotechnology—A Global Overview

The modern biotechnology industry was not born in the United States but rather in Europe in 1953. It was then that Dr. James Watson and Mr. Francis Crick of Cambridge University in the United Kingdom discovered the double helix structure of DNA. Following this discovery, they realized that if the genetic instructions for the manufacture of a desirable protein could be identified and inserted into the DNA of a living cell, then that cell would be able not only to manufacture the protein but also to pass on that ability to future generations of cells.[77] The practical utility of this discovery was significant in that it allowed for the mass production of rare but desirable proteins, usually drugs, through the use of living organisms as factories; and the "improvement" of the organisms themselves, usually by the addition to their DNA of a new gene which confers a desirable quality on the organism—pest-resistance to crops, for example.[78] Many of the original scientific discoveries that drive biotechnology were not made in the United States but rather in Europe, specifically Great Britain. However, the U.S., because of its well-developed venture capital system has been much more adept at commercializing those discoveries. This is evident in these tables from Philip Cooke's article "New Economy Innovation Systems: Biotechnology in Europe and the USA" that appeared in the December 2001 Industry and Innovation:

[77]"The Genetic Alternative: A Survey of Biotechnology." *The Economist*, April 30, 1988, p.5.
[78]Ibid.

Selected Key Biotechnology Innovations

Date	Innovation	Scientists	Country
1953	DNA structure	Watson/Crick	UK
1974	*In vitro* recombinant DNA	Cohen/Boyer	USA
1975	Monoclonal antibodies	Milstein/Kohler	UK
1977	DNA sequencing	Sanger et. al.	UK
1978	Polymerase chain reaction	Mullis	USA
1979	p53 Cancer gene	Lane	UK
1982	Cascade superfusion bioassay	Vane	UK
1985	DNA profiling	Jeffreys	UK
1988	H2-receptor antagonist	Black	UK
1996	Transgenic sheep	Wilmut	UK
1998	Antibody protein engineering	Winter	UK
1998	Nematode worm sequence	Sulston	UK

Source: Schitag et. al. (1998), BioIndustry Association (1999)

Key Innovations in Diagnostics

Date	Innovation	Country of origin
1972	Enzyme labels (ELISA)	Netherlands
1976	Flow-through membranes	UK
1979	Time-resolved fluorescence	UK
1980	Enzyme amplification	UK
1980	Chemoluminescence	UK
1980	Biosensors	UK/Sweden/USA/Japan
1984	DNA fingerprinting	UK
1985	PCR amplication	UK
1986	Immunochromatography	UK/USA
1991	DNA chip	UK/USA
1993	Lab on a chip	UK/USA

Source: DTI (1999), British In Vitro Diagnostics Association

Venture Capital Investments in New Technology Firms[79] (US$ millions)

Country	1995	1996	1997	Growth 1996-97 (%)	2004
USA	4,045	5,952	8,487	43	3,600
Europe	1,676	1,688	2,607	74	3,360
UK	800	696	1,253	72	450
Germany	181	242	379	82	290
Netherlands					24

The final table is also quite illustrative as it highlights the profound difference in U.S. and European venture capital investments in new technologies such as biotechnology in the late 1990s. The results of this new economy innovation system have been quite successful in the United States because as of 2001, there were 1,497 biotechnology firms

[79] European Venture Capital Association (1998) and Ernst & Young, Global Biotechnology Report 2005. 2004 figures are for biotechnology only.

in the U.S.[80] In addition to venture capital, this "new economy innovation system" is characterized by localization in or near innovative cities or urban agglomerations which host knowledge-driven clusters, and regionalization in states or sub-national administrative areas with benign or proactive policies towards the promotion of systemic innovation.[81] In contrast, Europeans trail in the commercialization of biotechnology because, despite scientific breakthroughs, their regional innovation system which is supported by extensive public sector enterprise support activities is not as successful as the U.S. venture-capital led model.[82]

From its inception, the biopharmaceutical sector in the United States has been influenced by two factors: foreign investment and geography. The biopharmaceutical industry started out as a sub-sector of the chemical industry and beginning in the 19th century was greatly shaped by advances in chemical engineering and basic chemistry that emanated from Europe, particularly Germany or later German scientists based in the United Kingdom. While the science was predominantly German, British firms dominated the production of chemicals during the first half of the 19th century. Foreign direct investment and the importation of this talent from Europe via immigration had more of an impact on the pre-WWI American chemical industry than any other US industry.[83] Indeed, some of America's most commercially successful pharmaceutical firms such as Pfizer and Merck were initially German in origin. Foreign influence has continued to this day with the recent influx of foreign investment from Swiss firms such as Novartis.

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[80]Ibid, p.5.
[81]Cooke, Philip. "New Economy Innovation Systems: Biotechnology in Europe and the USA." *Industry and Innovation*, December 2001.
[82]Ibid.
[83] Wallace, Lorna."Foreign Direct Investment Into the State of New Jersey." PhD Dissertation, New Jersey: Rutgers University Press, 1998.

Surprisingly, European pharmaceutical firms are leading the way in globalization. Genentech, a major U.S. biotechnology firm, is actually owned by the Swiss pharmaceutical firm Roche and in 1997, the formerly Swedish firm Pharmacia Corp. transferred its entire headquarters from London to New Jersey where it was joined by the French-German pharmaceutical firm Aventis in 1999. In particular, as part of its strategic plan, the Swiss pharmaceutical firm Novartis has been shifting more and more of its R&D to American biotechnology clusters. For example, Novartis has leased 764,000 square feet of lab space in Cambridge and invested $750 million to develop, equip, and staff what is now the Novartis Institutes for Biomedical Research, the lead research facility and global command center for the company's R&D efforts.[84] Dr. Daniel Vasella, Chairman and CEO of Novartis explained the company's rationale for locating in Cambridge: "Analysis shows that it is more and more difficult to attract and retain scientific talent, so we have to go where the talent is. Cambridge is a pool of scientific talent not found elsewhere in the world."[85] The vitality of America's biotechnology clusters due to the aforementioned success of its venture capital-led model is a major reason for this shift. However, there are other reasons. Biotechnology clusters depend upon pre-commercial R&D which is driven by the amount of funding for basic research. In this regard the United States far outpaces Europe as the National Institutes of Health's $23 billion annual budget for research grants—much of which are allocated to universities and hospitals—is about 50 times the amount devoted to such grants by all of the members of the European Union combined.[86] Europe also lags behind the U.S. in

[84]"Massachusetts: betting on biotechnology." *Plants Sites and Parks*, 29 (7): 78, January 2003.
[85]Halper, Deborah and Campbell, Kenneth. "Novartis is Opening Research Center in Tech Square." *Tech Talk*, May 8, 2002.
[86]Ibid.

adopting research-friendly regulations. For instance, Europe adopted an "orphan drug act," a provision designed to encourage research into treatments for rare diseases with certain market protection, in 2000—15 years after the U.S. did.[87] Political pressures in Europe from environmental activists fiercely opposed to the use of genetically modified animals for testing, an essential tool in biotechnology research, also works against the biotechnology industry in Europe.[88] These incentives make biotechnology clusters in the United States more vital than their European counterparts. This is evidenced by dramatic differences in the scale of the biotechnology industry in the U.S. relative to other locales:

Main International Bioscience Competitors, 2003[89]

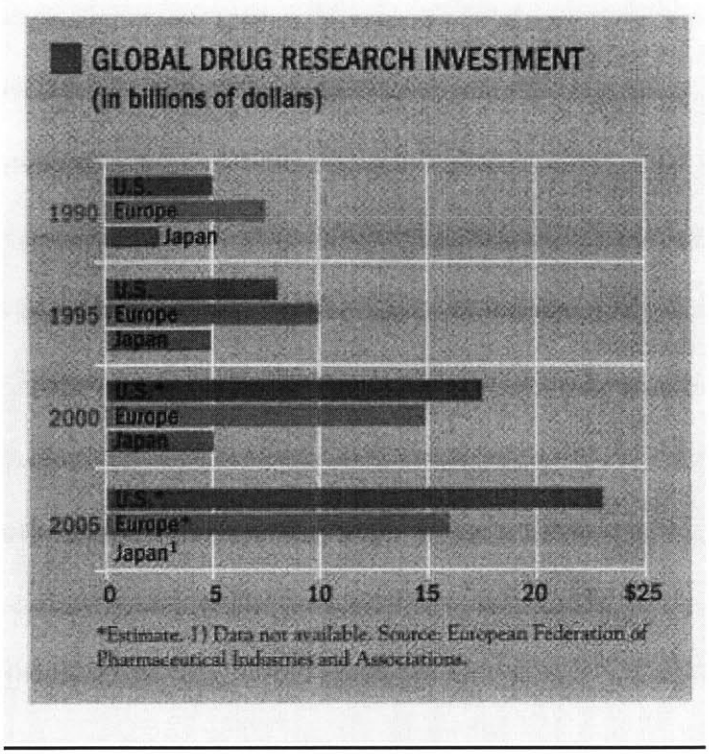
Country	Companies	Public Cos.	Market Cap. (billions $)	Revenues (billions $)	Employees	Pipeline Products
USA	1457	307	270.0	35.6	191,000	872
UK	331	46	12.4	4.0	22,000	194
Switzerland	129	5	9.6	2.6	8,000	79
France	239	6	.7	.4	9,655	31
Germany	369	13	.7	.7	13,386	15

However in Europe, the shift to innovation through biotechnology has been complicated by government interventions such as cost control measures, cut-backs on state-reimbursed pharmaceutical purchases, health care reform, and pressures on physicians to limit prescribing that have greatly decreased profit margins.[90] For example, in 1993, the German government imposed a five per cent price cut on prescription drugs and a two per cent price reduction on `over-the-counter' (OTC) medicines.[91] As monopoly purchasers of pharmaceuticals, Europe's government-run health care systems have pushed drug prices down 40% to 60% of U.S. levels, thereby making the American

[87]Ibid.
[88]King, Ralph and Moore, Stephen. "Swiss Stakes: Basel's Drug Giants are placing Huge Bets on U.S. Biotech Firms." *Wall Street Journal*, November 29, 1995.
[89] Derived from "Global Bioregions: Knowledge Domains, Capabilities and Innovation System Networks." Phil Cooke. *Industry and Innovation*, vol. 13, no. 4, p.440, December 2006.
[90]Ibid.
[91]Ibid.

market far more profitable.[92] In contrast, in the United States, the cost of prescription drugs is higher, doctors are more willing to prescribe innovative treatments, and direct-to-consumer advertising is not banned as it is in Europe.[93] Since most European pharmaceutical firms now generate most of their profits in the United States, they have been moving more and more of their R&D to the U.S. as well. As Dr. Daniel Vasella, the CEO of Novartis, a firm which generates 43% of its sales in the U.S. and less than one-third in Europe, notes: "There's no doubt that growth and profitability in a marketplace help determine where research investment goes. It's simple business logic."[94] The cumulative result of all of these factors has been the increasing globalization of the biopharmaceutical industry with the U.S. emerging as the global center for biotechnology R&D. This graph[95] demonstrates the dramatic shift in global drug research investment:

[92]"The Novartis Warning." *Wall Street Journal*, May 8, 2002.
[93]Capell, Kerry. "Novartis." *BusinessWeek*, May 26, 2003.
[94]Fuhrmans, Vanessa and Zimmerman, Rachel. "Leading the News: Novartis to Move Global Lab to U.S.—Swiss Drug Maker Follows Other European Companies Shifting Strategy Abroad." *Wall Street Journal*, May 7, 2002.
[95]Mullin, Rick. "Novartis shifts its R&D headquarters to the U.S." *Chemical Week*, May 15, 2002.



As is evidenced, through 1995, Europe had a significant lead in global drug research investment, but as the pharmaceutical industry has shifted more of its investments into biotechnology and the consequence of Europe's deleterious scientific and regulatory environment have become apparent that lead has abated. In 2000, Europe attracted only about 70% of the $24.3 billion in biopharmaceutical research investment that the U.S. did, a direct reverse of their portions of research dollars in 1990.[96] The critical impact of this trend is the relationship that has developed between small biotechnology start-ups and large pharmaceutical firms as it necessitates a focus on the large and small firms that are the most active stakeholders within a biotechnology cluster.

[96]Fuhrmans, Vanessa and Zimmerman, Rachel. "Leading the News: Novartis to Move Global Lab to U.S.— Swiss Drug Maker Follows Other European Companies Shifting Strategy Abroad," *Wall Street Journal*, May 7, 2002.

The biotechnology industry has evolved into a global biotechnology production system that also extends to areas beyond the United States. In particular, the manufacturing phase has shifted to developing countries that offer tax advantages. For example, in 2000, Schering-Plough announced that it would build four production and research units at Tuas Pharma Park in Singapore for a cost of $450 million.[97] Plans included a multi-product bulk manufacturing plant, a biotechnology sterile manufacturing facility, an oral solid dosage unit and an R&D facility.[98] At about the same time, Pfizer announced plans for a $350 million facility, also at Tuas, for the manufacture of active ingredients such as sildenafil (Viagra) and others drugs for angina and high blood pressure.[99] Singapore's streamlined investment approval apparatus, strong intellectual property protection, and highly educated workforce make it attractive as a production site. As the Singapore minister of health notes: "Singapore aims to become a strategic base for the world scale manufacture of pharmaceuticals, biopharmaceuticals and health care products. Singapore is also being developed as the regional hub for medical and health care services, with a strong research and development orientation, leading to linkages in the pharmaceutical and biotechnology industry."[100] The aspiration to be a global biotechnology R&D hub is evidenced in the government's creation of Biopolis, a dedicated science park that provides state-of-the-art lab facilities for biomedical sciences companies near research institutes and universities. As an inducement for foreign investment, Singapore's regulatory regime allows greater research freedom. For example, unlike in the United States, scientists in Singapore are free to explore the limits of stem

[97] Clay Boswell. "New Construction in Pharmaceutical Manufacturing," Chemical Market Reporter, June 18, 2001.
[98] Ibid.
[99] Ibid.
[100] Ibid

cell research. Singapore's efforts are being rewarded as in February 2003, Novartis launched a $160 million research institute in Singapore to discover drugs for tropical diseases such as dengue fever and multi-drug-resistant tuberculosis which afflicts the poorer areas of Africa and Asia.[101] Not to be outdone, Malaysia is developing "BioValley," a dedicated zone for biotechnology investment.

With regards to becoming an integral part of the global biotechnology production system, the most successful developing country vis a vis biomanufacturing is not in Asia but rather in the Caribbean. Puerto Rico has excelled as a production site for biopharmaceuticals. This began in 1976 when Congress created tax credits under Section 936 of the Internal Revenue tax for U.S. companies operating in U.S. territories to create jobs and investment from the mainland. Pharmaceutical companies used the tax credits to establish manufacturing plants in Puerto and by 1993, they employed 22,000.[102] As biotechnology has become an ever more significant component of pharmaceutical operations, Puerto Rico has also emerged as an important site for biomanufacturing. The credit was attractive to drug companies because their low per-unit raw material, manufacturing, and shipping costs made production at a remote site feasible, and the large profit margins they required to recover their costly research investments were covered by the credit.[103] Even after the Section 936 tax credit was eliminated in the mid-1990s, new tax laws were adopted to maintain the Puerto Rico's competitive position. Companies already operating under Section 936 were granted a 10-year grandfather period and companies can convert their operations to "controlled foreign corporations"

[101] "Business: Exotic pursuits; Drugs for the poor," The Economist, February 1, 2003.
[102] "Drugs-manufacturing jobs in Puerto Rico," Monthly Labor Review, March 1995.
[103] Ibid.

(CFCs), whose active income is not taxed in the US.[104] Puerto Rico then offers eligible companies a tax rate capped at 7%.[105] Alternatively, a company looking to expand its global presence can invest in Puerto Rico and channel the profits, tax-free, into investments in other countries.[106] The net result has been that Puerto Rico has remained a vital site for biopharmaceutical manufacturing. Between October 1996 and December 2002, jobs in the biopharmaceutical manufacturing sector have risen by over 5,500, according to Puerto Rican Industrial Development Company statistics and exports have more than quadrupled.[107] According to the Pharmaceutical Industry Association of Puerto Rico, 16 of the top 20 pharmaceuticals are produced in Puerto Rico.[108] In 2002 to 2003, over $2 billion was investment in biopharmaceutical manufacturing projects.[109] Recent investments include:[110]

[104] Lisa Jarvis. "Puerto Rico builds on initial advantage to promote growth in a post-936 environment," Chemical Market Reporter, February 24, 2003.
[105] Ibid.
[106] Ibid.
[107] Ibid.
[108] Ibid.
[109] Ibid.
[110] Ibid.

Recent Investments in Puerto Rico By Selected Major Companies

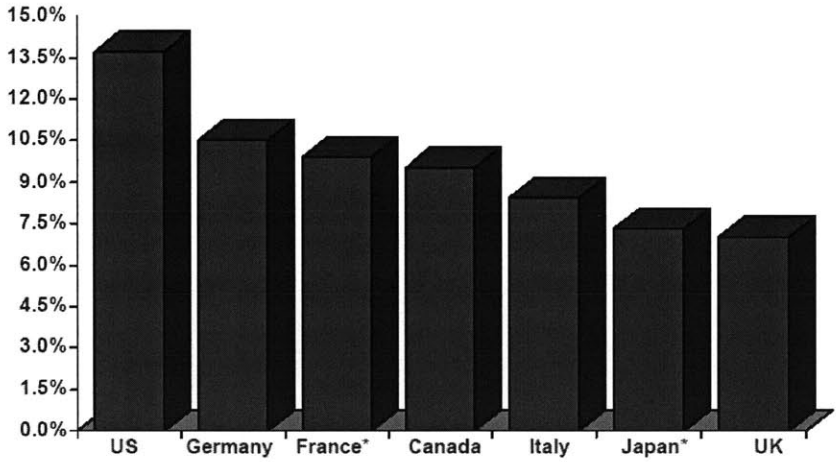
Company	Amount (in millions)	Type	Date
Merck	$360	biotechnology	Dec. '02
Abbott Labs	350	biotechnology	Oct. '02
Eli Lilly	450	biotechnology	June '02
Cordis (J&J)	20	medical instruments	June '02
Stryker	19	medical instruments/R&D	June '02
Pharmacia	103	pharmaceutical	May '02
Medtronic	24	medical instruments	May '02
Pharmacia	200	biotechnology	2002
Ortho	180	biotechnology	2002
Schering-Plough	60	pharmaceutical	March '01
J&J	12	pharmaceutical	Sept. '01
Abbott Labs	15	pharmaceutical	Oct. '00
Cardinal Health	19	pharmaceutical	April '00
Pfizer	75	pharmaceutical	June '99

Hence the development of a global biotechnology production system is having a significant impact upon the locational decisions of biotechnology firms in U.S. biotechnology centers such as Cambridge. As an affiliated territory, Puerto Rico clearly benefits from its proximity to the most vital biotechnology clusters and profitable pharmaceutical market in the world.

Part V: Biotechnology in the United States

The growth of biopharmaceuticals is being driven by a combination of demographics and rising health care costs. At 13.5%, the United States already has the highest health care costs in the world as a percentage of GDP:

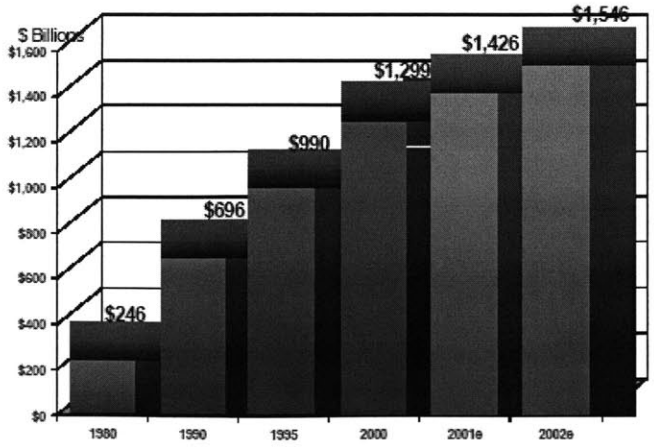
Comparison of Healthcare Spending as a Percentage of GDP



Source: Richard Seline. The Emerging Bioeconomy, December 2002.
(OECD Health Data, 1999; * Denotes 1998 Data.)

Moreover, the rate of growth of U.S. healthcare spending has been astounding. Since 1980, U.S. healthcare spending has increased by over 600%:

Growth of U.S. Healthcare Spending



Source: Richard Seline. The Emerging Bioeconomy.
(Center for Medicare and Medicaid Services—HCFA—2002)

The role of the health care system in the biotechnology industry has been acknowledged by leading academics such as Prof. Charles Cooney of MIT who points out that an affordable national health care system is vital to the industry as issues that pertain to the reimbursement of Medicare, and health care delivery determine whether or not it is possible to pay for the novel health care innovations derived from the industry.[111] According to Prof. Cooney, the lack of universal health care is a constraint because if one had universal health care, it would be possible to develop drugs for more people and this would stimulate more growth.[112] Anything that expands health care to more people creates more opportunity for the industry both locally and globally.[113] Thus, on the one hand, the absence of price controls that is characteristics of the U.S. health care system is attractive to biotech companies from around the world that realize tremendous profits in the U.S. market but it may also be constraining innovation in that it is not as profitable to create drugs for broader population groups since there is not as much market incentive.

The growth of biopharmaceutical clusters is also being driven by the fact that as the percentage of the world's population that is living longer increases due to health and medical breakthroughs and the many members of the baby-boom generation age, pharmaceutical and biotechnology firms expect the demand for medical therapies generated by biotechnology to grow.[114] The World Health Organization projects that the over 65 population will expand from just under 400 million in 1997 to more than 800 million by 2025.[115] This is a tremendous potential market for the products of

[111] Interview, Prof. Charles Cooney.
[112] Ibid.
[113] Ibid.
[114] Mitchell, Brandon. *Economic Development Challenges in the City of Cambridge: The Biotechnology Industry*, MCP Thesis, 2000, p.17.
[115] Ibid.

biopharmaceutical firms. It is especially lucrative because by 2002, 18-22% of the U.S. GDP will be comprised of health care and life sciences.[116]

The overall result of these trends is that biopharmaceuticals have become an enormous industry in the United States. Overall, the biopharmaceutical industry has generated $83.7 billion of total earnings in 2003.[117] This includes $29.5 billion in direct earnings and $54.2 billion in indirect earnings which in turn produced $24.4 billion in federal taxes.[118] Its impact on industrial research and development is especially large as the biotechnology industry was responsible for 8.5% of total industrial R&D in the nation in 2002.[119] This is due to the fact that the industry is extremely research and knowledge-intensive so biotechnology startups reinvest 10-20% of sales in research and development, a high proportion compared to other industries.

Between 1983 and 2003, total direct employment in the overall U.S. biopharmaceutical industry has grown from 231,700 to 406,700, a 75% increase.[120] Of this, as of 2003, approximately 282,300 were employed in Pharmaceutical and Medicine Manufacturing. This is a 23% increase over the 229,400 who were employed in this sector in 1993. In 2003, approximately 124,400 were employed in R&D in Life Sciences. This is a 41% increase over the 87,900 who were employed in this sector in 1993. Since 1983, when R&D employment was a mere 54,200, national employment growth in R&D has been 129% versus only 59% employment growth (177,500 in 1983) from the much larger pharmaceutical and medicine manufacturing. This indicates America's accelerating

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[116] Richard Seline presentation. The Emerging Bioeconomy: U.S. and Global Alignment of the Life Sciences. December 2002.
[117] United States Department of Commerce 2003: *A Survey of the Use of Biotechnology in U.S. Industry*, Technology Administration and Bureau of Labor Statistics, BEA, Economy.com, Milken Institute.
[118] Ibid.
[119] Ibid.
[120] Ibid.

advantage in the research-intensive components of the biopharmaceutical value chain. When direct employment impacts (406,700) are added to indirect employment impacts (1,351,800), the total employment impact is 1,758,500 jobs.[121] However, with an average annual wage of $72,600 in 2003, biotechnology workers who possess the most current skills are witnessing dramatically higher earning power than those with older skills and there is a substantial gap in earnings between those employed in research and development and those engaged in manufacturing.[122] Moreover, earnings in U.S. biopharmaceutical manufacturing are higher on average than all other manufacturing industry wages in the country. In 2002, production or non-supervisory employees in biopharmaceutical manufacturing averaged $777.00 per week while those in all manufacturing industries averaged $619.00 per week.[123] The Department of Labor estimates that in 2002, about 28 percent of all jobs in pharmaceutical and medicine manufacturing were in professional and related occupations, mostly scientists and science technicians; 18 percent were in management occupations, 12 percent were employed in office and administrative support, and 3 percent in sales and related occupations.[124] Approximately three out of every 10 jobs in the industry are in production occupations, including both low- and high-skilled jobs.[125] However, there is substantial regional variation of economic development impacts which sheds significant light on the optimal jobs mix in a biopharmaceutical cluster.

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[121] Ibid.
[122] Ibid.
[123] United States Bureau of Labor Statistics, U.S. Department of Labor, Career Guide to Industries, 2004-2005 Edition, Pharmaceutical and Medicine Manufacturing: http://www.bls.gov/oco/cg/cgs009.htm.
[124] Ibid.
[125] Ibid.

Part VI: The Dynamics of the Biotechnology Industry

Herein, I will address the question of exactly what is the biopharmaceutical industry and delineate its value chain. This is critical to understand how the biotechnology industry organizes itself as part of a regional innovation system. Moreover, I will point out the benefits of this pattern of organization for the biopharmaceutical industry. I will also address the question of how the biopharmaceutical industry has evolved in the Boston/Cambridge and Northeast Corridor areas by demonstrating how policies have been used in the United States to support the development of the biotechnology industry. I argue that the policy context in the United States is a critical factor in its success in evolving into a global center for the industry despite the fact that the science of biotechnology originated in Europe.

In 1973, biotechnology took an important step towards commercialization in the United States when a series of patent applications were filed by Professors Stan Cohen of Stanford University and Herb Boyer of the University of California at San Francisco.[126] These patents provided a technique for moving genes between organisms and transformed the basic science of molecular biology into commercially useful knowledge. Importantly, the timing of these discoveries coincided with a new era of active technology transfer by American research universities that relied on patenting scientific discoveries and then licensing the right to use these patents to firms to increase the commercialization of academic research.[127]

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[126]Feldman, Maryann. "The Locational Dynamics of the U.S. Biotechnology Industry: Knowledge Externalities and the Anchor Hypothesis." Prepared for the Dutch interuniversity research group *Technology and Economic Growth* conference on August 26-27, 2002, p.3.
[127]Ibid.

Biotechnology firms tend to cluster around universities, which are sources of basic scientific research.[128] This phenomenon is explained by Philip Cooke who reasons that in bioscience megacenters, private industry is not the research leader so it must locate near public research laboratories, particularly those associated with leading edge universities.[129] The firms benefit by gaining access to three distinct forms of knowledge spillover:

1) Anticipatory Knowledge: swift receipt of value-adding knowledge prior to its general release
2) Participatory Knowledge: timely availability of complementary local assets or capabilities
3) Precipitatory Knowledge: early access to local inventions, discoveries or innovations[130]

By collocating in close proximity to the research laboratories, the firms increase demand for the real estate in the area.

Biotechnology firms also cluster around universities because the technology has a long research phase before marketable products are produced. The basic science base in the university milieu is also a magnet for biotechnology entrepreneurs. This basic science output which has an economic value of its own tends to attract venture capitalists and intellectual property lawyers interested in commercializing the innovations of university researchers.[131] Moreover, many founders of biotechnology firms are university professors

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[128] Carey Goldberg. "Across the U.S., universities are fueling high-tech booms," New York Times, October 8, 1999.
[129] Philip Cooke. "Rational drug design, the knowledge value chain and bioscience megacentres." Cambridge Journal of Economics, May 2005.
[130] Ibid.
[131] Philip Cooke. "New Economy Innovation Systems: Biotechnology in Europe and the USA." Industry and Innovation, December 2001.

for whom the maintenance of academic relationships is important. Furthermore, university life science graduates serve as the source of many nascent biotechnology firms' employees. The networking and social capital that are fostered by proximity to major institutions of higher learning is critical to biotechnology organizations because they tend to thrive when they are a part of a localized ecosystem that comprises customers, talent pools, thought leaders, research centers and academia.[132] Biotechnology entrepreneurs benefit from intellectual, technological and social "spillovers" based on network interactions with other entrepreneurs, other scientists, financiers and people in the same business and with comparable mindsets to themselves.[133] Organizing in clusters around universities is regarded as a superior model by biotechnology firms because of the opportunities for trustful tacit-knowledge exchange made possible by the absence of bureaucratic watchdogs.[134] Moreover, the more collaborative atmosphere also made competition through new business formation from start-ups and spin-offs more common than in other settings, because new business opportunities and market niches could be spotted early. [135] Lastly, hospitals are also a critical component of biotechnology clusters in the United States as they provide testing services for biotech products going through the clinical trial phase. All of these stakeholders in the biotechnology industry need and compete for scare space within the biotechnology cluster which has the potential to significantly impact the real estate markets in the urban core where the biotechnology industry is situated.

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[132] John Dodge. "Boston area proves a lure for biotech sector," The Boston Globe, September 18, 2002.
[133] Philip Cooke. "New Economy Innovation Systems: Biotechnology in Europe and the USA." Industry and Innovation, December 2001, vol. 8, no.3, pp.267-289.
[134] Ibid.
[135] Philip Cooke. "New Economy Innovation Systems: Biotechnology in Europe and the USA." Industry and Innovation, December 2001, vol.8, no.3, pp.267-289.

The Biopharmaceutical Value Chain

How does the biotech industry organize itself regionally? It is an enterprise that requires a sustained physical presence in the urban core and face to face relationships with the universities, hospitals, and governmental entities that still reside in the urban core. In that sense, biotechnology is an example of the concept of *industrial filtering* which refers to the tendency of establishments to locate in metropolitan areas when they are new because proximity to the higher skilled, higher cost labor associated with metropolitan locations is relatively important; and because of the imperative of entrepreneurs retaining close ties with research centers and hospitals.[136] Likewise, according to the urban incubation hypothesis of Leone and Struyk:

> ...new, small manufacturing plants might be expected to concentrate in the older areas in central cities due to the ready availability of low cost easily divisible loft space and access to a number of services which the firm is unable to provide internally. Upon reaching maturity these plants might be expected to decentralize in keeping with well-documented relocation trends.[137]

In the case of biotechnology, the manufacturing does tend to relocate to cheaper locales. For example, in the United States, it is common for pharmaceutical firms to manufacture in Puerto Rico so as to take advantage of reduced costs, proximity to North American markets and preferential trade agreements with the United States. In the European context, Ireland has become a center for the manufacture of pharmaceutical products. However, the core research and development does not decentralize but tends to remain in the urban core because of the specific characteristics of the biotechnology industry.

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[136] Bingham, Richard, and Mier, Robert, eds. Theories of local economic development. (Newbury Park: Sage Publications, 1993), p.12.

[137] Robert Leone and Raymond Struyk. "The Incubator Hypothesis: Evidence from Five SMAs." *Urban Studies* (1976), vol. 13, pp.325-331.

Moreover, because biotechnology deals with fundamental research into the application of new scientific knowledge, that knowledge is highly tacit and non-codifiable so it is very difficult to transfer it abroad.

The significance of biotechnology vis a vis urban dynamics is also due to the unique process through which biotechnology products come to market. This process is evidenced in the biotechnology value chain:

Phase	Tasks	Time	Actors
1) Research	Product discovery; identification of product for commercialization	0-3 Years	Research Universities and Start-Ups
2) Development	Clinical Trials; Involves animal and human testing for the product's safety and efficacy; Government Review and Approval	3-4 Years	Governmental Regulatory Agencies; Research Universities and Start-Ups
3) Manufacturing	Mass Production	Variable	Large Pharmaceutical Firms
4) Commercialization	Marketing and Selling	5 Years	Large Pharmaceutical Firms

The Biotechnology Value Chain[138]

These actors organize as a cluster, a geographically proximate group of interconnected companies and associated institutions in a particular field, linked by commonalities and complementarities.[139] Unlike another knowledge-intensive industry such as software, biotechnology has a long production phase. It can take anywhere from 10 to 15 years for a product to make it to market—if it does at all—and the costs of bringing it to market

[138] November 25th 2002 interview with Mr. Glen Camiso, Biotechnology Project Leader, The Boston Consulting Group and Lourdes Pagaran. Determinants of Location and Competitiveness in the Biotechnology Industry: The Case of Massachusetts, MCP Thesis, MIT DUSP, 1993, p.21.

[139] Porter, Michael. On Competition. (Boston, MA: Harvard Business School Press, 1998), p.199.

can get as high as 800 million dollars.[140] It is important to note that government through federally-financed university research and regulatory agencies plays a critical role in the first two phases—research and development—which last as much as 7 years. This makes public policy important to the biotech industry. It also makes biotech even more urban because it is rooted for long periods during the R&D and testing phases. As the industry has become more science-intensive and innovation-driven, it has become harder to pick winners so a peculiar relationship has developed between small startups who do the R&D during the first 5-7 years and the large pharmaceutical firms who commercialize and manufacture the viable products. The startups identify those scientific breakthroughs that are most commercializable and are seeking to create enough value to be bought out by a large pharmaceutical firm that is able to leverage its ability to identify, access, harness, and effectively coordinate and deploy resources and capabilities from across the globe so as to bring the product to market. Manufacturing is particularly important to broad based economic development as it tends to employ less skilled employees who are a larger proportion of the labor market.

The Biotechnology Regional Innovation System

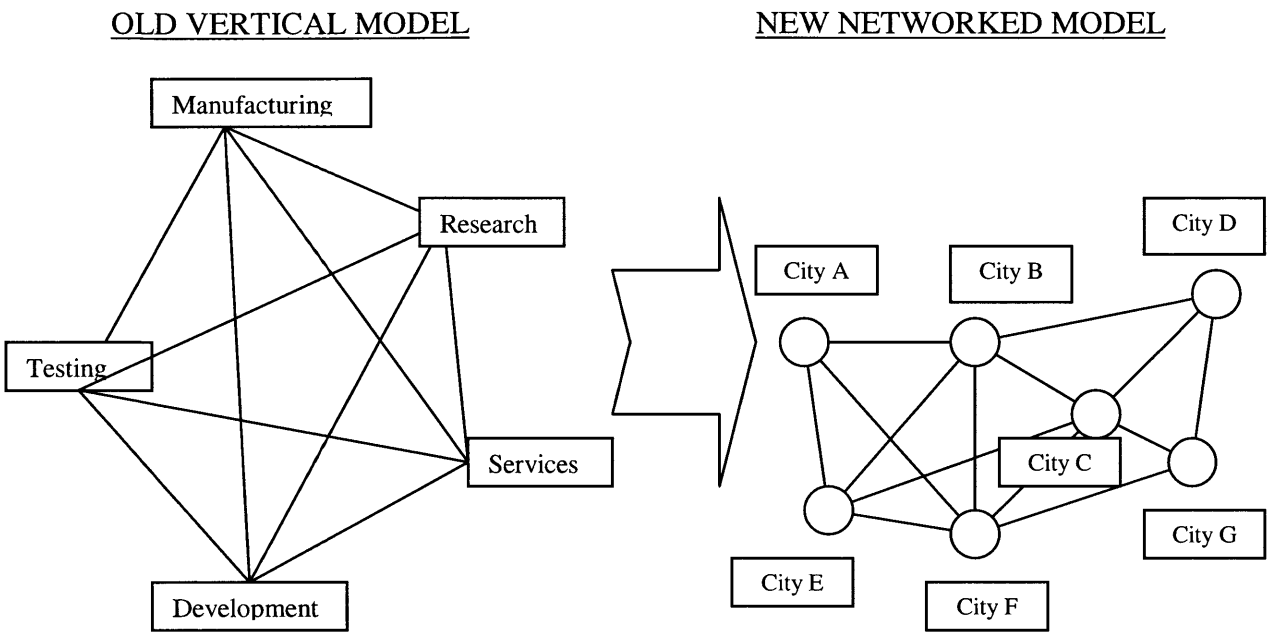
In the United States, the biopharmaceutical industry has experienced two distinct waves of development. The first wave as embodied by firms such as Genentech and Amgen involved the establishment of fully-integrated pharmaceutical-like firms with drug discovery, development, regulatory, sales and marketing activities all being done by

[140] Bill Fair. "Chasing Science: Can bioscience drive economic development? It depends." *The Scientist*, vol. 19, issue 8, April 25, 2005.

one company. This period of a vertically integrated business model roughly began with the establishment of Genentech in 1976, which was founded by MIT grad Robert Swanson, and ended in 1995 as the science of biotechnology became increasingly important and venture capital surged into the sector. In the mid-1990s, due to the aforementioned extensive R&D costs, a second wave of development began which entailed a shift from the vertically integrated model to one of specialized niche players in the overall value chain. Large pharmaceutical firms switched from internal research and development to cherry picking the most commercializable technologies from small biotech startups. The startups specialized in R&D and the large firms used their manufacturing, marketing and distribution capabilities to bring the product to market. In essence, this second wave of development has become associated with a *network model* as specific operations, administrative functions, regulatory activities, and marketing are done within one area while research, testing, clinical trials and manufacturing are done in other locales. This business model shift towards networks has strengthened the power of polynuclear regions and made presence within a strong regional system of innovation a significant advantage for biopharmaceutical companies. The economic and commercial logic behind linking the core competencies within one city with other competencies in another city signals a shift in the traditional model of economic development: no longer does a city have to have all the ingredients intrinsic to the success of a particular industry but the ability to complement the capabilities of other regional actors can boost regional economic development for all stakeholders.[141] Across a region, clusters, institutions and talent now network beyond their local community as part of a larger, multi-tiered

[141] Dr. Cinda-Herndon King and Richard Seline. "Prospects for a Bioeconomy: The Biomedical Industry and Regional Economic Development." November 1, 2000.

production process that is local, regional and ultimately global in scope. This shift is reflected below:



The growing importance of the science of biotechnology in the pharmaceutical industry has led to the advent of biopharmaceuticals as a symbiotic relationship has developed between biotechnology firms and pharmaceutical firms, both foreign and American. Whereas pharmaceutical firms used to perform most of their R&D internally, the science of chemistry has been supplanted by the science of biotechnology and they are increasingly dependent upon the biotechnology industry for the key innovations that are necessary to effectively compete in the marketplace against cheaper generic alternatives. The pharmaceutical industry's response has been to focus on delivering better products through biotechnology. In many respects, a biotechnology firm is a "pharmaceutical firm without sales" as it performs the research innovations that are vital to the pharmaceutical

industry. Between 1980 and 1992, the proportion of total projects at pharmaceutical companies that were related to biotechnology rose from 2% to 33% and has risen further since.[142] By 1995, two-thirds of the roughly 3,000 drug compounds under development were being engineered in biotech labs.[143] Although most of the major pharmaceutical companies have internal biotechnology capabilities, self-sufficiency is not regarded as a viable strategy because of the competitiveness of the marketplace.[144] Rather, the modern pharmaceutical industry is built on "cherry picking" new product concepts from a large pool of ideas; a strategy that requires constant interaction with and physical presence near the universities, research institutes, and biotechnology firms in major research clusters such as Boston and San Diego.[145]

The American biopharmaceutical industry has a strong presence in the Northeast Corridor which stretches from Boston, down through the New York and New Jersey and into the Washington, DC/Baltimore, MD metropolitan areas. Most of the world's leading traditional pharmaceutical firms have their world or U.S. headquarters, or in the case of foreign-based multinational enterprises, their FDI, in this areas. These firms have generally located their principal research laboratories and product launching plants either on-site or in close proximity to their offices. As new products achieve commercial economies of scale and manufacturing production processes become increasingly routine,

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[142]Williams, Gwilym. "Biotechnology market development in Ireland: Issues of strategy, risk, and partnership." *Irish Marketing Review*, 1998 and U.S. and International Research and Development: R&D Patterns by Sector. www.nsf.gov/statistics/seind98/access/c4/c4s2.htm

[143]King, Ralph and Moore, Stephen. "Swiss Stakes: Basel's Drug Giants are placing Huge Bets on U.S. Biotech Firms." *Wall Street Journal*, November 29, 1995.

[144]Williams, Gwilym. "Biotechnology market development in Ireland: Issues of strategy, risk, and partnership." *Irish Marketing Review*, 1998.

[145]Ibid.

they are frequently outsourced to lower-wage regions such as Puerto Rico and Ireland.[146] Conversely, foreign firms are increasingly relocating their knowledge-intensive activities such as research and development operations to the United States. However, it should be noted that downstream functions such as manufacturing and marketing contribute substantially to a region's economic well-being through growth in regional incomes, maintenance of a relatively good income distribution and contribution to a quality-living environment.

Both biotechnology startups and large firms tend to cluster in distinct locales as part of a regional innovation system of the Northeast Corridor. For example, 80% of large pharmaceutical employment is in the New York-New Jersey metropolitan area while the Boston-Cambridge metropolitan area is the second largest biotechnology cluster in the United States (Life Science 2000). Three of the ten largest U.S. biotech companies—Biogen, Genzyme, and Charles River Laboratories—in terms of sales are located in the Boston metropolitan area and seven of the ten largest U.S. pharmaceutical companies by sales rank are located New York-New Jersey metropolitan area including Merck, Bristol-Myers-Squibb, Pfizer, American Home Products, Warner Lambert, Schering Plough and Pharmacia & Upjohn, Inc.[147] The complementary functionality and rootedness of these key nodes in the biotechnology value chain demonstrates one of the ways that the polynuclear Northeast Corridor functions as a regional innovation system to the benefit of this knowledge-intensive industry.

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[146] Marialba Martinez. "Merger of Pharmaceutical, Biotechnology Industries could spell disaster for P.R." Caribbean Business, July 15, 2004.

[147] Cortright, Joseph and Mayer, Heike. *Signs of Life: The Growth of Biotechnology Centers in the U.S.* The Brookings Institution Center on Urban and Metropolitan Policy, (2002), p.6.

While each geographical node serves a distinct function within the biotechnology value chain, the fact that all three areas have world class hospitals and universities that attract funding and conduct the testing that is critical to the vitality of the industry makes the region especially significant to the biopharmaceutical industry. The Boston, NY-NJ, and Washington, DC-Baltimore, MD metropolitan areas complement each other while providing ready access to networks of customers (patients); milieux of innovation (major research centers); and labor markets for both employers and employees. In the Northeast Corridor's regional innovation system, the federal government which is predominantly based in the Washington, DC-Baltimore, MD metropolitan area acts as the major knowledge regulator (FDA), and knowledge funder (NIH grants); research institutes (NIH) and research universities (MIT and Harvard) act as knowledge producers; and firms both large (NY-NJ) and small (Boston-Cambridge is the predominant center for startups) act as knowledge users and appliers. Knowledge is diffused through the easy interaction that the polynuclear region facilitates.

Cambridge/Boston is a part of the Northeast Corridor, a regional agglomeration wherein the biopharmaceutical value chain is organized around distinct nodes each with their own specialized function.

The Northeast Corridor

In Cambridge, universities serve as an anchor that attracts research funding and cultivates startups; in NY/NJ, large pharmaceutical firms are the dominant actor; and in the Washington, DC/MD metropolitan area, large governmental institutions such as the NIH are the key actor. Through these industry stakeholders, the biopharmaceutical industry has distinct regional economic development impacts as delineated above. The impacts are not uniform but vary depending upon the character of each area. What is uniformly evident is that the proportion of employment in research and development relative to manufacturing has been increasing thereby demonstrating that there is shift afoot towards the more knowledge intensive jobs remaining in the Northeast Corridor. The one partial

exception is the NY/NJ metropolitan area and even there with substantial number of manufacturing jobs, employment has been growing fastest in research and development.

The 2002 NAICS data in the below table summarizes much of the aforementioned impacts and scale of the industry:

2002 NAICS DATA FOR SELECTED METROPOLITAN AREAS[148]

LOCATION	Estab.	Value of Shipments ($1000)	Annual Payroll ($1000)	Paid Employees
WASHINGTON D.C. AREA				
Virginia				
325411 Medicinal & botanical mfg	5	D	D	(1000-2499)
325412 Pharmaceutical preparation mfg	6	511,613	53,865	1,476
325413 In-vitro diagnostic substance mfg	3	D	D	(100-249)
325414 Biological product (except diagnostic) mfg	3	D	D	(100-249)
Maryland				
32541 Pharmaceutical & medicine mfg	45	1,487,351	227,766	4,497
325412 Pharmaceutical preparation mfg	19	D	D	(1000-2499)
325413 In-vitro diagnostic substance mfg	11	416,242	121,943	2,148
325414 Biological product (except diagnostic) mfg	13	835,293	51,274	1,029
Washington-Baltimore-Northern Virginia, DC-MD-VA-WV Combined Statistical Area				
32541 Pharmaceutical & medicine mfg	50	D	D	(2500-4999)
325412 Pharmaceutical preparation mfg	21	D	D	(1000-2499)
325413 In-vitro diagnostic substance mfg	12	D	D	(1000-2499)
325414 Biological product (except diagnostic) mfg	13	D	D	(1000-2499)
Baltimore-Towson, Maryland Metropolitan Statistical Area				
32541 Pharmaceutical & medicine mfg	20	557,479	143,486	2,917
325412 Pharmaceutical preparation mfg	11	D	D	(1000-2499)
325413 In-vitro diagnostic substance mfg	3	D	D	(1000-2499)
Bethesda-Frederick-Gaithersburg				
32541 Pharmaceutical & medicine mfg	16	809,541	64,331	1,161
325413 In-vitro diagnostic substance mfg	7	D	D	(250-499)
325414 Biological product (except diagnostic) mfg	4	D	D	(500-999)

[148] Data derived from US Census. D indicates withheld to avoid disclosing data of individual companies; data are included in higher level totals.

NEW YORK AREA

New York				
325411 Medicinal & botanical mfg	29	839,449	59,362	1,388
325412 Pharmaceutical preparation mfg	96	13,941,900	872,852	17,589
325413 In-vitro diagnostic substance mfg	9	573,600	115,089	1,774
325414 Biological product (except diagnostic) mfg	6	132,618	19,553	434
New York-Newark-Bridgeport, NY-NJ-CT-PA Combined Statistical Area				
325411 Medicinal & botanical mfg	53	D	D	(5000-9999)
325412 Pharmaceutical preparation mfg	167	D	D	(25k-49k)
325413 In-vitro diagnostic substance mfg	11	D	D	(2500-4999)
325414 Biological product (except diagnostic) mfg	8	D	D	(250-499)
New York-Newark-Edison, NY-NJ-PA Metropolitan Statistical Area				
325411 Medicinal & botanical mfg	50	2,668,574	247,309	5,434
325412 Pharmaceutical preparation mfg	150	22,403,160	2,121,637	36,315
325413 In-vitro diagnostic substance mfg	11	D	D	(2500-4999)
325414 Biological product (except diagnostic) mfg	8	D	D	(250-499)

BOSTON AREA

Massachusetts				
325411 Medicinal & botanical mfg	16	94,195	28,296	492
325412 Pharmaceutical preparation mfg	33	2,275,658	320,273	5,316
325413 In-vitro diagnostic substance mfg	11	459,283	100,643	1,976
325414 Biological product (except diagnostic) mfg	15	803,589	78,337	1,334
Boston-Cambridge-Quincy, MA-NH Metropolitan Statistical Area				
325411 Medicinal & botanical mfg	15	D	D	(250-499)
325412 Pharmaceutical preparation mfg	27	D	D	(5000-9999)
325413 In-vitro diagnostic substance mfg	9	D	D	(1000-2499)
325414 Biological product (except diagnostic) mfg	13	D	D	(1000-2499)
Boston-Worcester-Manchester, MA-NH Combined Statistical Area				
325411 Medicinal & botanical mfg	15	D	D	(250-499)
325412 Pharmaceutical preparation mfg	33	D	D	(5000-9999)
325413 In-vitro diagnostic substance mfg	10	D	D	(1000-2499)
325414 Biological product (except diagnostic) mfg	15	D	D	(1000-2499)

In many respects, each geographical node has a dominant institution—Boston (universities and startups); New York-New Jersey (large pharmaceuticals); and Washington, DC-Baltimore, MD (government) that also influences urban dynamics. In the Northeast Corridor, the biotechnology value chain looks as follows:

Phase	Tasks	Time	Actors	Location
1) Research	Product discovery; identification of product for commercialization	0-3 Years	Research Universities; Research Institutes and Start-Ups	Boston/Cambridge Metropolitan Area and Washington, DC-Baltimore Area
2) Development	Clinical Trials; Involves animal and human testing for the product's safety and efficacy; FDA Review and Approval	3-4 Years	Research Universities and Start-Ups	Boston/Cambridge Metropolitan Area and Washington, DC-Baltimore Area
3) Manufacturing	Mass Production	Variable	Large Pharmaceutical Firms	New York/ New Jersey Metropolitan Area
4) Commercialization	Marketing and Selling	5 Years	Large Pharmaceutical Firms	New York/ New Jersey Metropolitan Area

The Northeast Corridor Biotechnology Regional Innovation System

As of 2002, over $18 billion has been committed by U.S. regions to stimulate the development of life science activities in research, infrastructure, and commercialization.[149] During the following eight years, over 22 million square feet of new space was planned for development to serve as research space, wetlabs, commercialization incubators, production, and manufacturing; and there is still a shortage in certain real estate markets such as New York City.[150] It is common for bioscience

[149] Richard Seline presentation. The Emerging Bioeconomy: U.S. and Global Alignment of the Life Sciences. December 2002.
[150] Ibid.

space to be two to four times more expensive than standard office space so its urban impact will be dramatic.[151] This impact is especially profound due to the highly specialized character of bioscience facilities which must be constructed to handle heavy lab equipment and toxic materials. Larger open spaces, higher ceilings, and reinforced floors are typically required to accommodate the needs of the industry.[152] Consequently, in order to recoup the investment, the developer must charge premium rents.

The impact of the biotechnology industry is also manifested through government agencies such as the National Institutes of Health which is based in Bethesda, Maryland and research universities such as Johns Hopkins University which ranks first in NIH funding. Washington, DC and Baltimore are a regulatory and public funding node in the Northeast Corridor regional innovation system. The Washington-Baltimore Consolidated Metropolitan Statistical Area had a population of 7.6 million in 2000, making it the fourth-largest metropolitan area in the United States. The labor market is strong as in addition to Johns Hopkins, there are 12 biological institutions granting life science PhDs and total NIH financial support flowing to the Washington, D.C., area is more than $1 billion annually; and a large number of scientists and professionals have extensive experience in the industry. Washington is also home to BIO, the industry's principal trade association. Still, the impact of Johns Hopkins on Baltimore is restrained by the fact that it is not a vital center for biotechnology startups due to the university's cultural emphasis on basic research and scholarly publication, as well as the lack of a local supportive and innovative environment. This is similar to the manner in which European universities

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[151] Bill Fair. "Chasing Science: Can bioscience drive economic development? It depends." *The Scientist*, vol. 19, issue 8, April 25, 2005.
[152] Brandon Mitchell, Economic Development Challenges in the City of Cambridge: the biotechnology industry, MCP Thesis, 2000, p.54.

until recently have been constrained in their capacity to commercialize their innovations. However, government's role as regulator, funder, and researcher is immense—NIH accounts for more than $28 billion in grants alone not accounting for FDA grants and Department of Defense spending on biotechnology concerns such as biosecurity. That impact is felt in Bethesda, MD where NIH is based. It is particularly evident in Maryland cities of Gaithersburg, Rockville and Frederick in the Hagerstown-Washington County, MD area that is home to over 300 biotechnology companies.[153] Currently, it is estimated that approximately 15,000 biotech workers are employed in Maryland firms, 17,000 in Federal labs, and 9,000 in universities for a total of almost 50,000 dedicated biotechnology researchers and supporting staff (MdBio 2001). The region has significant expertise in genomics which is a legacy of the publicly funded Human Genome Project that was based in the area.

The New York–New Jersey Consolidated Metropolitan Statistical Area includes the New York, Newark, and New Haven metropolitan areas and adjacent counties in Connecticut and Pennsylvania. The area had a year 2000 population of 21 million, making it the largest metropolitan area in the United States. Although the area receives over $1.3 billion in NIH funding and is home to 10 major academic medical centers, 4700 life scientists, and more than 20 other research institutions, the scarcity of commercial lab space has inhibited the further growth of the industry. There is presently only 112,000 square feet of commercial lab space in the city compared to over 1.5 million square feet available in Boston and Cambridge.[154] Large pharmaceutical firms

[153] Thom Hallock. "Biotech: A Wealth of Choices." Business Facilities, April 2004.

[154] Ivan Oransky and Richard Gallagher. "New York City: Start Spreading the News." *The Scientist*, November 2004.

serve as the anchors in the New York-New Jersey metropolitan area. These include Merck, Pfizer, Bristol-Myers-Squibb, American Home Products, Warner Lambert, Schering Plough, and Pharmacia & Upjohn—all of which are top ten pharmaceutical companies that are headquartered in New York City. Three of the world's pharmaceutical giants – Pfizer, Bristol-Myers Squibb, and Forest Laboratories – are actually located within one square mile of each other in midtown Manhattan. In this market, the large pharmaceutical firms and a number of startups that anchor this node in the biopharmaceutical chain compete primarily over office space. Pfizer has recently announced expansion plans—it will spend about $1 billion to renovate its Manhattan headquarters, buy additional office space, and add staff over the next 15 years, including 2,000 jobs to be added by 2009.[155] Another firm, Eyetech moved from a 16,000-square foot office space in the garment district to a 60,000-square foot space in the Reuters Building in Times Square.[156] Columbia University would like to expand its biotechnology operations into neighboring Harlem but there is mounting tension over gentrification. All of this has put space in Audobon Biomedical Science and Technology Park, New York City's first university-related research park at a premium. Yet the region's advantage is definitely more for large pharmaceutical firms who gain access to a deep pool of management expertise and the financial capital—investment banking markets are distinct from venture capital markets—that are crucial when they enter the marketing and commercialization phases to acquire and manage startups.

The Boston metropolitan area, which has a population of over 5.8 million, is the major research center and a center for affiliated startups generated by research

[155] Jack Lucentini. "Kings of the Hill: Big Players in Pharma Choose Manhattan for their Headquarters." The Scientist, November 2004.
[156] Ibid.

universities that serve as the academic anchors of the region. It is the second largest biotechnology cluster in the United States after the San Francisco Bay Area—a polynuclear region in its own right. Boston alone receives more NIH funding—over $1.4 billion—than any other metropolitan area in the country. There are 25,000 employees just in biotech, not counting medical devices and hospitals and ten research institutions in the Boston area are among the top 100 institutions that receive NIH funding. MIT and Harvard serve as critical stakeholders in that firms such as Novartis are willing to pay a premium to locate in close proximity to their milieux of innovation and young startups often must be close for purposes of access to both social capital and physical equipment that is key to commercialization during a firm's incipient phases of development. Indeed, the vitality of the biotechnology industry in the Boston metropolitan area is leading to a space crunch that is impacting economic development. For example, in Boston, the Longwood Medical Area is nearly out of biotechnology space and according to a report by Spaulding & Slye Collins, a Boston real estate firm, East Cambridge and Boston's Longwood Medical Area are simply running out of room.[157] Although there are plenty of lab space alternatives in the suburbs, untested locations are seen as a huge risk, and for the majority of life science companies, the need to be in close proximity to the labor pools and resources of MIT, Massachusetts General Hospital, or Harvard Medical School is critical. The importance that firms attach to proximity to biotechnology clusters such as Cambridge and Boston is evidenced by the existence of 6.8 million square feet of biotech lab space in Cambridge, of which over 5 million was built in the last five years; and an

[157] Jeffrey Krasner. "Biotechnology/In the pipeline," The Boston Globe, August 28, 2002.

additional 1.9 million square feet of lab space in Boston.[158] As of 2002, in the City of Cambridge, the biotechnology lab sector accounts for 20% of all of the commercial real estate and this will grow another 30% in the next two years.[159] The value that firms place on this space is demonstrated by the 2002 decision of Swiss drug-maker Novartis to lease 764,000 square feet of lab space in Cambridge and invest $750 million to develop, equip, and staff what will become the Novartis Institutes for Biomedical Research, the lead research facility for the company. Daniel Vasella, Chairman and CEO of Novartis explained the company's rationale for locating in Cambridge: "Analysis shows that it is more and more difficult to attract and retain scientific talent, so we have to go where the talent is. Cambridge is a pool of scientific talent not found elsewhere in the world."[160] According to Mayor Michael Sullivan, the current vacancy rate for laboratory space in the entire City of Cambridge is only 2%.[161] All of this is having a dramatic impact upon local economic development as there is now a renewed emphasis on developing brownfields—tracts of land that have been polluted and abandoned—in previously depressed areas as biotech centers.

The aforementioned phases of the biotechnology value chain are greatly influenced by both the political dynamics of the regulatory process which is based in the Washington, D.C.-Baltimore, MD metropolitan area where elected officials and the FDA and NIH make national health care policy; and over 28 billion dollars in pre-commercial R&D—33% of which is absorbed by Northeast Corridor research institutions in Boston,

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[158] David Clem, Lyme Properties, presentation to MIT Center for Real Estate and Thomas Palmer, Jr., "Experts Expect Growth of Boston-Area Biotechnology Industry to Continue," The Boston Globe, October 10, 2002.
[159] Thomas Palmer, Jr., "Experts Expect Growth of Boston-Area Biotechnology Industry to Continue," The Boston Globe, October 10, 2002.
[160] Deborah Halper and Kenneth Campbell. "Novartis is Opening Research Center in Tech Square," Tech Talk, May 8, 2002.
[161] Ibid.

New York-New Jersey, Washington, D.C.-Baltimore, Maryland, and Philadelphia—that is allocated from NIH alone annually.

Likewise, the private sector has been active in the biotechnology industry in the Northeast Corridor. This is evidenced by its status as a focal point for venture capital investments in the industry:

1995-2004 Venture Capital Investments in Biotechnology in Northeast Corridor[162]

	Boston Metro	Annual % of Regional Venture Capital Total	NY/NJ Metro	Annual % of Regional Venture Capital Total	DC/MD Metro	Annual % of Regional Venture Capital Total
1995	$188,000,000	25.6	$27,000,000	5.3	$22,000,000	6.6
1996	$229,000,000	19.8	$18,000,000	2.3	$35,000,000	5.9
1997	$248,000,000	15.8	$73,000,000	5.7	$61,000,000	11.4
1998	$269,000,000	11.2	$113,000,000	6.6	$56,000,000	5.0
1999	$305,000,000	5.6	$54,000,000	1.1	$37,000,000	1.7
2000	$441,000,000	3.8	$453,000,000	4.2	$126,000,000	2.2
2001	$524,000,000	9.9	$377,000,000	10.3	$148,000,000	6.8
2002	$542,000,000	19.3	$394,000,000	27.1	$176,000,000	16.0
2003	$802,000,000	26.9	$482,000,000	33.5	$99,000,000	11.6
2004	$715,000,000	23.0	$353,000,000	23.4	$258,000,000	26.8

The fact that the biotechnology industry accounts for approximately a quarter of the total venture capital invested in each region demonstrates the attractiveness of these nodes within the Northeast Corridor as centers for biotechnology activity.

[162] PricewaterhouseCooper's MoneyTree Survey. http://www.pwcmoneytree.com/moneytree/index.jsp

Summary

The fact that the science of biotechnology originated in Europe but that the United States has had far greater success in commercializing biotechnology is critical to this study. This is because different areas are subject to different governmental policy milieux and different governmental policy choices that will be explored below. Moreover, in terms of its value chain, biotechnology firms tend to cluster around universities so as to benefit from the knowledge spillovers of government-financed pre-commercial research and development. Clustering around universities also gives the firms access to the scarce, highly-trained scientific and technical personnel—many of whom maintain employment relationships with large research universities—that are critical to the development of the industry. Secondly, the long research phase (8-10 years) of the industry's innovation requires that firms remain rooted in particular locales for several years before they realize a benefit on their investments. Thirdly, organizing as part of a regional cluster allows firms to capitalize upon the social capital and relationships with professionals and venture capitalists that is critical to the success of a biotechnology firm. Fourthly, an important benefit is being able to engage in tests and trials at nearby hospitals as that is a key activity for the biotechnology industry. Understanding the increasingly regional organizational pattern of the biotechnology industry is essential to an analysis of critical locational trends in the Cambridge area.

In this section, I have also explored in detail how the biopharmaceutical industry in the Northeast Corridor of the United States has evolved to organize itself as part of a coherent regional innovation system. We have learned that each of the nodes/cities serves a critical function in the biopharmaceutical value chain. Key nodes in this system are

Boston/Cambridge and Washington, D.C. (start-ups, research and development, and policymaking); and NY/NJ (manufacturing and commercialization). At each node in the regional innovation system, there are dominant stakeholders who drive cluster development and impact the urban milieu. This regional innovation system has proven to be quite successful in the United States and is a major reason why the Northeast Corridor is a major global epicenter for the biopharmaceutical industry. This is in significant part due to the fact that it acts as a global magnet for top scientific talent and facilitates their interaction across the biopharmaceutical value chain.

Part VII: Biotechnology in Massachusetts

The United States is a global leader in biotechnology and Massachusetts is a critical focal point for biotechnology innovation in the American milieu. As is evident in this timeline, Massachusetts has played a significant role in the evolution of the biotechnology industry:

Life Sciences Innovation Timeline[163]

1721— Dr. Zabdiel Boylston, at the urging of Cotton Mather, inoculated the local population with a new technique to halt the spread of smallpox.
1846— William Morton, a dentist at Massachusetts General Hospital, revolutionized the practice of surgery by demonstrating the use of ether as an anesthetic. Today Massachusetts General continues to innovate, and is the single largest recipient of NIH funding in the state.
1914— Theodore Williams of Harvard University was the first of more than 30 Massachusetts scientists to win a Nobel Prize.
1926— William T. Bovie, a Harvard physicist working at Brigham & Women's Hospital, conducted research that resulted in the creation of an electrosurgical knife, used to treat tumors that previously were considered inoperable.
1938— Cardiac surgery is elevated to a new level with the first successful congenital cardiovascular defect surgically corrected by Dr. Robert Gross at Children's Hospital.
1952— Paul Zoll of Beth Israel Hospital was the first to succeed in using electrical stimulation to restart a patient's heart, and the pacemaker was born. More than half a century later, Zoll Medical Corporation is still a leader in resuscitation devices.
1962— James Watson of Harvard shared a Nobel Prize with Francis Crick and Maurice Wilkins, for the discovery of the double helix, the molecular structure of DNA.
1962— University of Massachusetts Medical Center in Worcester was founded, helping to create a second anchor of the cluster in Massachusetts.
1978— Walter Gilbert of Harvard and Phillip Sharp of MIT helped found Biogen, the first of Massachusetts' biopharmaceutical companies, to focus on human gene research to improve healthcare. Both men went on to receive Nobel Prizes.
1979— Indicative of the life sciences cluster spreading from its original base, Boston Scientific, is formed. With a market capitalization of over $23 billion, the company is now the largest life sciences company in the state.
1985— Genzyme Corporation had its first drug, Ceradase, approved to treat Gaucher disease, an extremely rare condition afflicting less than 10,000 people worldwide.

[163] Super Cluster. 2007. A joint publication of the Massachusetts Technology Collaborative, PriceWaterhouseCoopers and the New England Healthcare Initiative.

1986— Researchers at the Massachusetts Eye & Ear Infirmary isolated the first human cancer gene.
1988— Building on the early research in genomics, molecular geneticists at Harvard received the first U.S. patent for a genetically altered mouse.
1996— Wyeth Pharmaceuticals acquired Genetics Institute, becoming the first large pharmaceutical company to establish significant manufacturing operations in Massachusetts.
1999— The sequencing of the human genome is completed, due in large part to the Whitehead Institute/MIT Center for Genome Research.
2002— Novartis establishes operations in Massachusetts, illustrating a trend of traditional pharmaceuticals setting up operations in the state.
2003— The Broad Institute, a research collaboration among Whitehead Institute, MIT and Harvard University, was founded, where genomics research flourishes.
2006— Craig Mello, of the University of Massachusetts Medical Center shared the Nobel Prize with Andrew Fire for their discovery of RNA interference, which paved the way for future medical advances

The state of Massachusetts is also noted as a major training ground for biotechnology talent. According to the National Science Foundation, 14 Massachusetts universities granted 609 PhDs in biology, chemistry and chemical engineering in 2005.[164] The state's status as a talent incubator for life sciences is evident as it leads the nation in life sciences PhDs granted per 100,000 people:

Life Science PhDs Granted Per 100,000 People[165]

	Biology	Chemistry	Chemical Engineering
Massachusetts	6.51	2.05	0.90
Maryland	3.88	0.45	0.30
New York	3.13	0.72	0.28
North Carolina	3.10	0.92	0.16
Pennsylvania	2.22	0.89	0.48
California	2.05	0.81	0.28

[164] Ibid.
[165] Ibid.

Massachusetts is also an epicenter for the capital—both public and private—that drives the biotechnology industry. In 2005, the state received approximately $2.3 billion in National Institutes of Health funding, a figure that amounts to almost 10% of the U.S. total.[166]

Massachusetts' Share of NIH Funding by Funding Institute, 2005[167]

Institute	MA Amount ($ millions)	% MA Share
National Institute of Allergy and Infectious Diseases	$371	16%
National Cancer Institute	$311	15%
National Heart, Lung, and Blood Institute	$278	12%
National Institute of General Medical Sciences	$188	8%
National Institute of Diabetes and Digestive and Kidney Disorders	$181	8%
National Institute of Neurological Disorders and Stroke	$133	6%
National Human Genome Research Institute	$94	4%
National Institute of Aging	$91	4%
National Institute of Mental Health	$88	4%
All Other Institutes	$538	23%
Total—All Institutes	$2,273	100%

The state is second only to California in the total amount of NIH funding that it receives:

[166] Ibid.
[167] Ibid.

Top 10 NIH Grantee States, 2005[168]

Rank (Total Funding	State	Amount of Funding Received ($ millions)
1	California	$3,301
2	Massachusetts	$2,273
3	New York	$2,021
4	Maryland	$1,764
5	Pennsylvania	$1,452
6	Texas	$1,150
7	North Carolina	$1,078
8	Washington	$813
9	Illinois	$734
10	Ohio	$717

However, according to 2005 figures, the state of Massachusetts leads the nation in per capita NIH funding:

2005 NIH Funding Per Capita

State	Amount of Funding Per Capita
Massachusetts	$353
Maryland	$316
Connecticut	$131
Washington	$129

[168] Ibid.

North Carolina	$124
Rhode Island	$123
Pennsylvania	$117
Vermont	$108
New York	$105

Of the 5,193 grants and contracts that were awarded throughout the state in 2005, almost 90% were used for research projects and the remainder went to fellowships, training and construction.[169]

Massachusetts has been successful in attracting not only public funding but also private sector support for the biotechnology industry. Between 2005 and 2006, venture financing of Massachusetts' life sciences companies increased 43% to $1.1 billion.[170] Approximately 2/3 of the deals--$755 million—were in the biotechnology sector involving companies targeting cancer, autoimmune diseases, and diabetes. The remaining deals involved medical devices and equipment companies--$292 million—and healthcare service companies--$37.5 million.[171] It is important to note that while venture capital investment has grown recently, it is still only equivalent to 50% of the funding levels of that of the NIH, which demonstrates the importance of government financing to the biotechnology industry.

As of 2001, approximately 8% of the world's total pipeline of biopharmaceutical drugs came from the 280 companies headquartered in Massachusetts.[172] The 280 biotech

[169] Ibid.
[170] Ibid.
[171] Ibid.
[172] MassBiotech 2010: Achieving Global Leadership in the Life Sciences Economy. Massachusetts

companies are a figure that represent a tripling from 1992, and 230 of those companies were actually founded in Massachusetts so a significant percentage—roughly 20%--were drawn to the state from outside locales.[173] Between 1996-2001, employment in the biotechnology industry grew 10% annually and contributed roughly half of the new industrial jobs in the state of Massachusetts.[174] This growth has been driven by the innovative capacity of Massachusetts biotechnology companies, which is evidenced below:

Selected List of FDA-Approved Massachusetts Biotechnology Products[175]

Company	Product	Used For
Abiomed	BVS-5000	Cardiac assistance for patients with failing hearts
Anika Therapeutics	Staarvisc II	Ophthalmic surgeries
Biogen, Inc.	Avonex	Multiple sclerosis
Biogen, Inc.	Intron A	AIDS-related Kaposi's sarcoma
/Schering Plough		Chronic hepatitis B and C
Biopure Corporation	Oxyglobin	Anemia
Curis, Inc.	OP-1 Implant	Bone fractures and defects
/Stryker Corporation		
DUSA Pharmaceuticals	Levulan	Actinic keratoses, skin lesions
/Berlex		
Exact Sciences	PreGen-26	Detection of colorectal cancer
Genentech, Inc	Nutropin Depot	Pedriatic growth hormone deficiency
/Alkermes, Inc.		
Genzyme Corporation	Carticel	Articular cartilage injuries
	Ceredase	Type 1 Gaucher disease
	Renagal	Hyperphosphatemia
	SepraFilm	Antiadhesion in surgery
	Synvisc	Osteoarthritic knee pain
	Thyrogen	Thyroid cancer
	Welchol	LDL cholesterol
GTC Biotherapeutics	Recombinant	Blood disorder
/Fresenius	Human Serum	
The Medicines Company	Angiomax	Coronary thrombosis
Millennium Pharma.	Campath	B-cell chronic lymphocytic leukemia
/ILEX Oncology, Inc.		
Millennium Pharm.	Integrilin	Acute coronary syndrome
/Schering Plough		
Organogenesis, Inc.	Apligraft	Diabetic foot ulcers

Biotechnology Council, 2002.

[173] Ibid.

[174] Ibid.

[175] Derived from MassBiotech 2010: Achieving Global Leadership in the Life Sciences Economy. Massachusetts Biotechnology Council, 2002.

/Novartis		
Sepracot, Inc.	Xopenex	Asthma
Serono, Inc.	Gonal-F	Infertility
	Rebif	Multiple sclerosis
	Saizen	Pedriatic growth hormone deficiency
	Serostim	AIDS wasting
Vertex Pharma.	Agenerase	AIDS/HIV
GlaxoSmithKline		
Wyeth	BeneFIX	Hemorrhagic episodes
	Neumaga	Low platelet counts
	ReFacto	Hemophilia

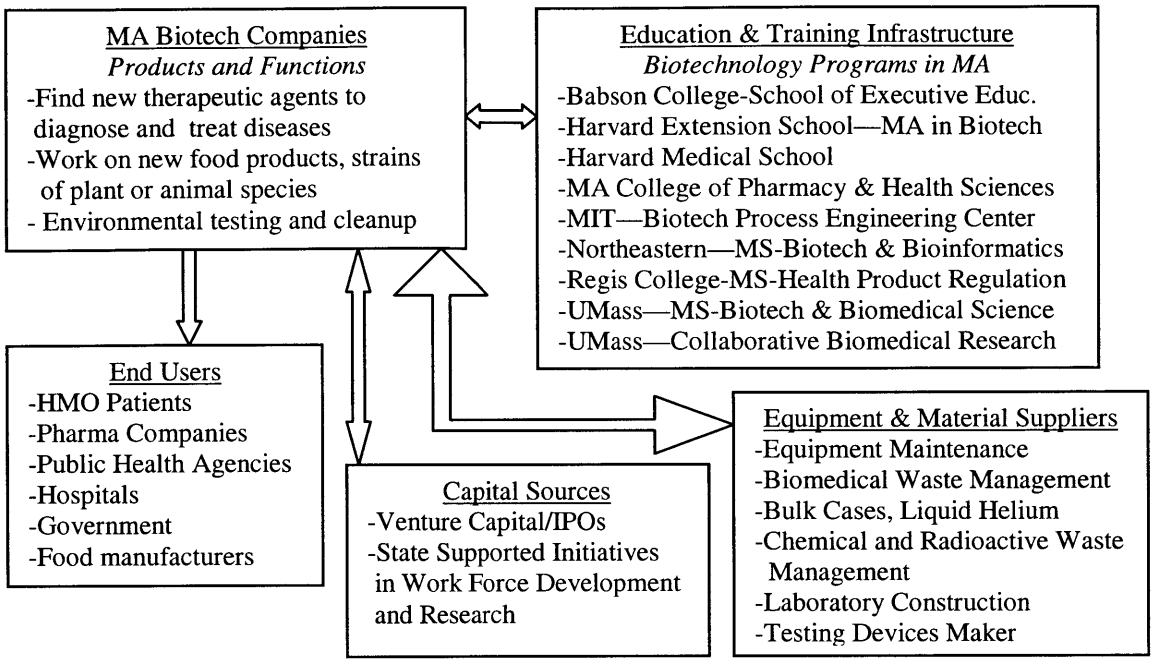
Between 2001 and 2005, employment in the biotech sector has grown by 20.9% and generated 3,400 new jobs for the Massachusetts economy.

Biotechnology Employment in MA, 2001-2005

Sector	2001	2002	2003	2004	2005	% Change 2001-2005
Biotechnology	16,300	17,300	17,100	18,800	19,700	20.9%

The Massachusetts biotechnology cluster is part of an ecosystem that, in addition to myriad companies, also includes related equipment and materials suppliers, world class end users/clients, capital sources, and perhaps most significantly world-renowned educational institutions that provide the human capital so critical to innovation in the biotechnology sector. The cluster is organized as follows:

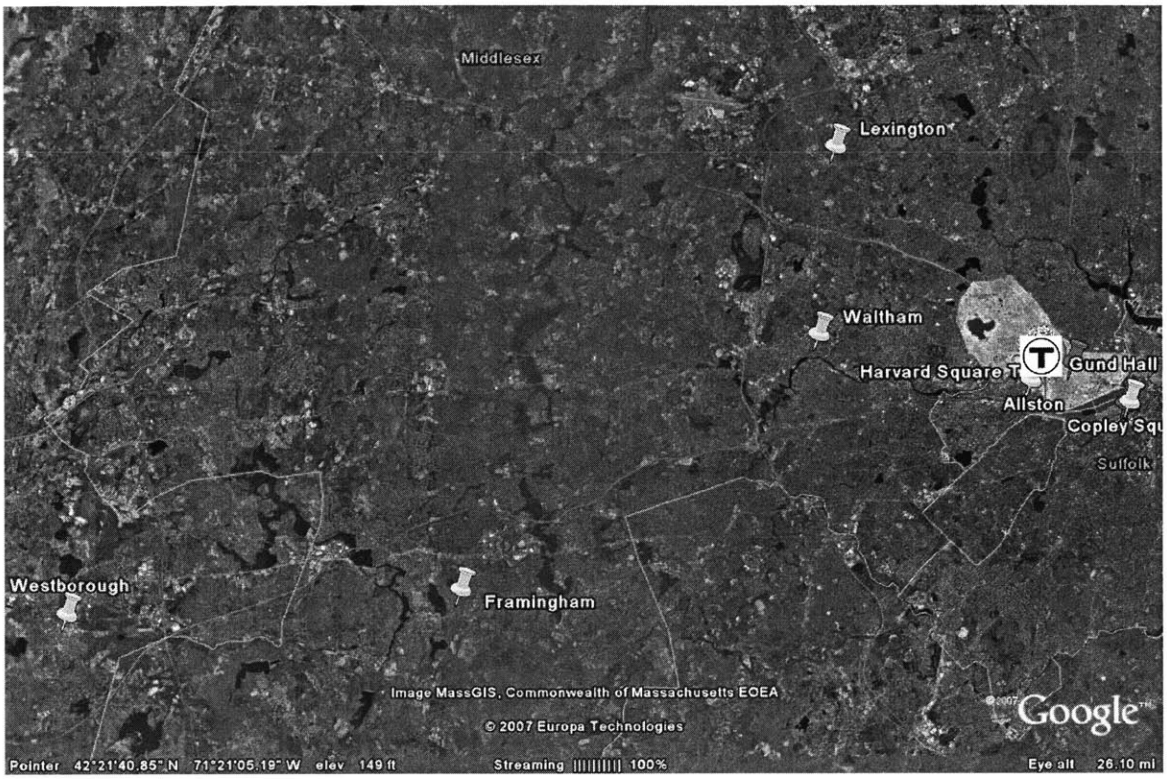
Massachusetts Biotechnology Cluster[176]



As shall be explored, areas throughout Massachusetts have begun to develop as biotechnology clusters with Cambridge as the preeminent biotech cluster in the region. As this map shows, Westborough, Framingham, Waltham and Lexington are in such close proximity to Cambridge that commuting between these areas is relatively easy:

[176] Breznitz, Shiri. Manufacturing Biotechnology in Massachusetts. MassBenchmark. 2006. vol 8, issue 1.

Cambridge/Boston Metropolitan Area and Adjacent Biotechnology Clusters



While Cambridge has retained its status as the epicenter of the biotechnology industry, particularly for the larger companies that can afford to purchase large plots of real estate, a hub and spoke locational pattern is developing in the area's biotechnology industry. Just as in New York City, lower-income, "bus and trainers" must migrate from Brooklyn, Queens, the Bronx, etc. into Manhattan for jobs due to the high cost of living in the urban core, so too as is evidenced in the discussion below, smaller firms or the manufacturing arms of large firms that require access to large plots of land are migrating from the hub—Cambridge--to the spokes—Westborough, Framingham, Waltham and Lexington. In that sense, the biotechnology industry in the Boston/Cambridge metropolitan area is being further regionalized such that new, less costly mini-clusters of biotechnology are emerging around Cambridge.

This trend towards the development of mini-clusters around Cambridge is evidenced by the number and variety of biotechnology firms that are currently located in the aforementioned areas:

Biotechnology Firms in Surrounding Mini-Clusters[177]

Framingham	Waltham	Lexington
Ariston Pharmaceuticals, Inc. 205 Newbury Street, Suite 407 Framingham, MA 01701	Adnexus Therapeutics, Inc. 100 Beaver Street Waltham, MA 02453	Abt Associates Clinical Trials 181 Spring Street Lexington, MA 02141
Artisan Pharma Inc. 161 Worcester Road, Suite 301 Framingham, MA 01701	AstraZeneca R&D 35 Gatehouse Drive Waltham, MA 02451	ActivBiotics 110 Hartwell Avenue Lexington, MA 02421
GTC Biotherapeutics, Inc. 175 Crossing Blvd. Framingham, MA 01702	BG Medicine, Inc. 610N Lincoln Street Waltham, MA 02451—1002	Antigenics, Inc. 3 Forbes Road Lexington, MA 02421
Life Science Insights 5 Speen Street Framingham, MA 01701	Cato Research Bay Colony Corporate Center, 1100 Winter St. Waltham, MA 02451	ApoConsult LLC 1139 Massachusetts Lexington, MA 02420
P.P. Manufacturing Corporation 175 Crossing Boulevard, Suite 200 Framingham, MA 01702	Confluent Surgical, Inc. 101 A First Avenue Waltham, MA 02451	Aptuit Consulting, Inc. 91 Hartwell Ave. Lexington, MA 02421
Panacea Clinical Research 19 Checkerberry Lane Framingham, MA 01702	Decision Biomarkers 150 Bear Hill Road Waltham, MA 01701	CoNCERT Pharmaceuticals, Inc. 99 Hayden Ave., Suite 100 Lexington, MA 02141
The GI Company, Inc. 1661 Worcester Rd. Suite 204	Decision Resources, Inc. 260 Charles St.	Critical Therapeutics, Inc. 60 Westview Street

[177] MassBio Database.

Framingham, MA 01701	Waltham, MA 02453	Lexington, MA 02421
Transport Pharmaceuticals 161 Worchester Road Suite 402 Framingham, MA 01701	Dynogen Pharmaceuticals, Inc. 52 Second Avenue Waltham, MA 02451	Cubist Pharmaceuticals, Inc. 65 Hayden Avenue Lexington, MA 02421
	Epitome Biosystems 100 Beaver Street Waltham, MA 02453	Cytomyx, LLC One Ledgemont Center, 128 Spring Street Lexington, MA 02421
	Eyegate Pharmaceuticals Inc. 100 Beaver Street, suite 200 Waltham, MA 02453	EPIX Pharmaceuticals, Inc. 4 Maguire Rd. Lexington, MA 02421
	Faber Daeufer & Rosenberg PC 950 Winter Street Waltham, MA 02451	Fresenius Biotech North America, Inc. 99 Hayden Avenue Lexington, MA 02420
	GPC Biotech Inc. 610 Lincoln Street Waltham, MA 02451	GulfStream Bioinformatics Corp. 99 Hayden Avenue Lexington, MA 02421
	I-Therapeutix, Inc. 235 Bear Hill Rd., Suite 301 Waltham, MA 02451	Hypnion, Inc. 500 Patriot Way Lexington, MA 02421
	Intelligent Bio-Systems, Inc. 34 Bear Hill Road Waltham, MA 02451-1002	Indevus Pharmaceuticals, Inc. 33 Hayden Avenue, Suite 200 Lexington, MA 02421
	Interleukin Genetics, Inc. 135 Beaver Street Waltham, MA 02452	MGI PHARMA, Inc. 44 Hartwell Ave. Lexington, MA 02421
	LabPros, Inc. 201 Jones Road, Suite 102 Waltham, MA 02451	NitroMed, Inc. 125 Spring Street Lexington, MA 02421

	Maxiom Group, Inc. 1601 Trapelo Road, Suite 145 Waltham, MA 02451	Predictive Biosciences, Inc. 92 Hayden Ave. Lexington, MA 02421
	Minerva Biotechnologies Corp. 6th Flr Rosenstiel Bldg., M/S 029, 415 South Street Waltham, MA 02454-9110	Synta Pharmaceuticals Corp. 45 Hartwell Avenue Lexington, MA 02421
	Oscient Pharmaceuticals 1000 Winter Streer, Suite 2200 Waltham, MA 02451	TransForm Pharmaceuticals, Inc. 29 Hartwell Avenue Lexington, MA 02421
	OXiGENE, Inc. 230 Third Ave Waltham, MA 02451	
	PAREXEL International Corp. 195 West Street Waltham, MA 02154-1116	
	Pericor Science Inc. 100 Beaver Street Waltham, MA 02453	
	Phase Forward, Inc. 880 Winter Street Waltham, MA 02451	
	Protein Forest, Inc. 100 Beaver Street, Suite 210 Waltham, MA 02453	
	Proteon Therapeutics, Inc. 200 West Street Waltham, MA 02451	
	Repligen Corporation 41 Seyon Street, Bldg # 1 Suite 100	

	Waltham, MA 02453	
	Thermo Electron Corporation 81 Wyman St. Waltham, MA 02454	
	Trine Pharmaceuticals, Inc. 78 Fourth Ave. Waltham, MA 02451-1624	
	WaveRx, Inc. 300 Bear Hill Road Waltham, MA 02451	

As this table shows there are at least 8 biotechnology firms in Framingham, 29 in Waltham and 19 in Lexington. Moreover, Waltham is home to a major venture capital firm in the form of Polaris Venture Partners and a professional service ecosystem of intellectual property lawyers such as Morse, Barnes-Brown & Pendleton.

Part VIII: Biotechnology in Cambridge

Cambridge, Massachusetts, a city of 101,355 people, with an area of 7.1 square miles is located along the Charles River across from Boston. It is the 5th most populous city in the state of Massachusetts with a median family income of $65,511, which is well above the national average of $46,326.[178] However, family purchasing power (adjusted for cost of living) is only $39,370.[179] Although the cost of living is notoriously high, compared to other biotechnology clusters—San Francisco has a media family income of $70,772 with family purchasing power of $24,074; and New York has a media family income of $45,788 with family purchasing power of $26,575—Cambridge is actually a bargain relative to those other locales for biotechnology professionals who elect to work in the city.[180] This data supports Prof. Cooney's assertion that although Cambridge is expensive it is more affordable than California.[181] More importantly, from the author's perspective, the geography of the area with Harvard University and MIT in close proximity, and Boston and Cambridge well-integrated through mass transit supports consistent physical interaction and the development of social capital amongst the cluster stakeholders. This in turn drives the innovation that is central to the success of the biotechnology industry.

Overall, Cambridge is the dominant biotechnology and life science/health care agglomeration in the Boston metropolitan area as it accounts for 30% of firms but 60% of employment which indicates that the larger, more successful firms such as Novartis are

[178] http://money.cnn.com/magazines/moneymag/bplive/2006/snapshots/PL2511000.html
[179] Ibid.
[180] Ibid.
[181] Interview with Charles Cooney, February 8, 2007.

located in Cambridge along with a healthy number of startups.[182] Indeed at 217 employees, the average employment of Cambridge firms is more than twice as high as the overall average in the industry and Boston has less than 4% as much employment as Cambridge.[183] Spinoffs from biotechnology have already had a distinct impact in East Cambridge's Kendall Square. Because of the Human Genome Project and the presence of the MIT-affiliated Whitehead Institute/MIT Center for Genome Research, Kendall Square in East Cambridge has become a focal point for biotech research on gene-derived drugs, therapies, and diagnostics.[184] Particularly after the lifting of rent control in 1994, the downside of the gene boom for longtime residents of Cambridge has been that wealthy entrepreneurs and well-paid employees of pharmaceutical companies are helping to drive up rents and house prices.[185] Indeed it was out of concern with overdevelopment and gentrification in East Cambridge and to promote more affordable housing in the area that the Pitkin Petition was filed in 1997 which led to an 18 month moratorium on development in excess of 20,000 square feet in the area. The moratorium was combined with an effort to promote the development of more affordable housing in Cambridge. Thus the biotechnology industry has played an increasingly significant role in both the economics and politics of the City of Cambridge. Moreover, the Pitkin Petition highlights the different role that local government plays for biotechnology clusters at different stages of development. In spite of the Pitkin Petition, and the absence of any monetary incentives, the biotechnology industry has continued to remain in Cambridge because of the talent basis. In contrast, communities that need growth such as nearby Boston resort

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[182] Breznitz, S.M. and Anderson, W. Boston Metropolitan Area Biotechnology Cluster. Canadian Journal of Regional Science, vol. 28-2, pp.249-264.
[183] Ibid.
[184] Kimberley Blanton. "Gene Pool," The Boston Globe, October 10, 1999.
[185] Ibid.

to friendlier regulation and a more active approach including infrastructure improvements[186] so as to induce firms to locate there.

The biotechnology industry's genesis in Cambridge was a function of the central role played by Harvard University and the Massachusetts Institute of Technology in attracting and credentialing the talent that the industry depends upon. Both universities have also been highly successful in winning research funding, particularly from federal sources such as NIH, and following the 1980 passage of the Bayh-Dole Act, that research has been actively commercialized through numerous start ups established by academics and alumni. As Prof. Charles Cooney has noted: "Companies locate in Cambridge because of the density of academic institutions which provides people and technology at multiple levels—management, science, labs, faculty advisors."[187] That perspective is reinforced by Estella Johnson of the Cambridge City Government's Community Economic Development Department who believes that Cambridge offers firms proximity and a knowledge base that is critical along with what she contends is an easy to use permitting process—she thinks 18 months is faster than in other locales—due to the local government's experience in that area.[188] Along with the talent in Cambridge, there is easy access to venture capital and there are also numerous supporting and related industries ranging from waste disposal companies and microscope manufacturers to law and accounting firms that specialize in biotechnology.[189] The density of academic and professional institutions and relationships with the people therein, makes it "sticky" for

[186] Interview with Thomas Finneran, January 18, 2007.
[187] Interview with Charles Cooney, February 8, 2007.
[188] Interview with Estella Johnson, January 29, 2007.
[189] Breznitz, Shiri. Manufacturing Biotechnology in Massachusetts. MassBenchmark. 2006. vol 8, issue 1.

firms in Cambridge. They continue to stay in Cambridge so as to continue to cultivate those relationships and capitalize on that social capital.

The role of universities in the Cambridge biotech ecosystem bears deeper exploration. Prof. Robert Langer, one of 13 Institute professors at MIT and a world-renowned expert in bioengineering argues that universities and their staff contribute by licensing technology, advising students who start companies, serving on different boards and training students.[190] However, it should be noted that even his lab of 100 people, which gets $7 million annually is 60% funded by the National Institutes of Health.[191] Still, MIT is particularly active with regards to licensing technology. According to Andrea Schievella, who handles biotechnology patents as part of a 4 member "biobunch" team at the MIT Technology Licensing Office, biotechnology is hugely important to MIT as 160 (40%) of the university's 400 new invention disclosures each year are in biotech and 20-25 companies are spun out each year.[192] The MIT TLO licenses the technology that MIT owns and as part of that process it hires patent attorneys to help process patent applications for student and faculty entrepreneurs. According to Ms. Schievella, who has been with the MIT TLO for 2 and a half years, big companies come to Cambridge to cherry pick (ideas and smaller companies) and physically having them all in the same area is huge as the social capital and networking generated facilitates the development of more companies and the overall growth of the industry.[193] The role of the TLO is to contribute to the growth of biotech by facilitating the establishment of new startups, and

[190] Interview with Robert Langer, January 31, 2007.
[191] Ibid.
[192] Interview with Andrea Schievella, February 9, 2007.
[193] Ibid.

providing/licensing new technologies that support them.[194] This includes helping inventors by paying for all the patent application costs—prior art searches, marketing, preparation of licensing agreement, etc.—and making a match with the appropriate attorneys.[195] As the author sees it, this process is highly iterative and involves the development of personal relationships that are difficult to replicate outside of the Cambridge milieu. These relationships facilitate the information gathering that is of central importance to a knowledge-based industry such as biotechnology. That along with the prospect of access to federal government-financed research incubated in a world class university that is actively seeking to commercialize its innovations is a powerful inducement for biotechnology firms to locate in Cambridge.

Location and geography are also important initially to firms as Cambridge is close to prominent teaching hospitals such as Massachusetts General Hospital where clinical trials are conducted. Elliott Hillback, Genzyme's Senior Vice President for Corporate Affairs, makes the case that universities are not the only inducement for firms to locate in Cambridge.[196] In addition to the sheer number of biotechnology firms that both compete and cooperate and the power of university connections, another powerful inducement for firms is that the hospital network is extremely strong with regards to the vitality of their research and patient arms and the amount of NIH funding that they receive.[197] Universities are not enough as there is a need for the collaboration of the medical community for product ideas and trials.[198] According to Mr. Hillback: "It is very hard to replicate this. You can't just bring in a bunch of firms as firms by themselves are not

[194] Ibid.
[195] Ibid.
[196] Interview with Elliott Hillback, March 9, 2007.
[197] Ibid.
[198] Ibid.

enough. You need a medical and a university side. The medical side is an attraction for the really good firms. It's a chicken and egg dilemma."[199] Prominent hospitals in close proximity include Massachusetts General Hospital, Beth Israel Deaconess, Dana-Farber Cancer Institute, and Brigham & Women's Hospital. Thus part of the talent advantage that Cambridge enjoys is found not only in its universities but in the hospitals of the metropolitan milieu. Yet the fact that Mr. Hillback took note of the NIH funding that hospitals in the area receive is indicative of the powerful indirect role played by public funding of research as part of what makes the Cambridge metropolitan area so attractive to biotechnology firms.

Cambridge also has the distinction of having some of the most well-educated residents in the nation. 65.1% of residents have a bachelor's degree or higher compared to 33.2% in Massachusetts and 24.4 in the United States generally.[200] Undoubtedly, this high level of educational attainment is due to the presence of two of the world's leading academic institutions: MIT and Harvard, which at 7,864 and 10,068 people respectively, are the city's largest employers.[201] Along with these institutions, Cambridge is home to many important technology firms including Lotus Development Corporation and Akamai. Although manufacturing was the most important part of the Cambridge economy until the early 20th century, followed by information technology until the 1990s, today, education, health care and biotechnology dominate the economy. In particular, Kendall Square and East Cambridge, which had been the center of the city's

[199] Ibid.
[200] City of Cambridge, Massachusetts Demographics and Socioeconomic Profile. Cambridge Community Development Department, 2003.
[201] City of Cambridge Community Development Department.

manufacturing, have become the geographical locus of the biotechnology sector as old factories are converted into lab and office space.

An examination of shifts in the top 25 employers in Cambridge demonstrated the growing importance of biotechnology to the Cambridge economy. In 1995, 2000 and 2006, the top employers in Cambridge were as follows:[202]

Top 25 Cambridge Employers: 1995

RANK	NAME OF EMPLOYER	NATURE OF BUSINESS	EMPLOYEES
1	HARVARD UNIVERSITY	EDUCATION	10,300
2	MASSACHUSETTS INSTITUTE OF TECHNOLOGY	EDUCATION	8,188
3	CITY OF CAMBRIDGE	GOVERNMENT	5,305
4	MT AUBURN HOSPITAL	MEDICAL	2,007
5	POLAROID	PHOTO and OPTIC EQUIPMENT	1,829
6	ARTHUR D. LITTLE, INC.	RESEARCH and DEVELOPMENT	1,317
7	BOLT, BERANEK and NEWMAN	RESEARCH and DEVELOPMENT	1,281
8	LOTUS DEVELOPMENT CORPORATION	COMPUTER SOFTWARE	1,165
9	DRAPER LABORATORY	RESEARCH and DEVELOPMENT	1,091
10	STAR MARKET	RETAIL	868
11	YOUVILLE HOSPITAL	MEDICAL	810
12	CRIMSON TRAVEL/THOMAS COOK	TRAVEL SERVICES	780
13	CAMP, DRESSER, MCKEE	ENGINEERING	645
14	U. S. DEPARTMENT OF TRANSPORTATION	GOVERNMENT	600

[202] Ibid.

15	RAYTHEON ENGINEERING	CONSTRUCTION	590
16	BIORAN	CLINICAL TESTING SERVICES	525
17	CAMBRIDGE TECHNOLOGY PARTNERS	MANAGEMENT CONSULTING	518
18	COMMONWEALTH ENERGY SYSTEMS	UTILITY	504
19	GENETICS INSTITUTE	RESEARCH and DEVELOPMENT	500
20	STRIDE RITE	FOOTWEAR	499
21	BIOGEN	BIOTECHNOLOGY	463
22	GENZYME	BIOTECHNOLOGY	450
23	LESLEY COLLEGE	EDUCATION	440
24	ABT ASSOCIATES	RESEARCH and DEVELOPMENT	394
25	HARVARD COOPERATIVE SOCIETY	RETAIL	350
TOTAL			41,419

Top 25 Cambridge Employers: 2000

RANK	NAME OF EMPLOYER	NATURE OF BUSINESS	EMPLOYEES
1	HARVARD UNIVERSITY	EDUCATION	8,128
2	MASSACHUSETTS INSTITUTE OF TECHNOLOGY	EDUCATION	7,102
3	CITY OF CAMBRIDGE	GOVERNMENT	2,931
4	MT AUBURN HOSPITAL	MEDICAL	2,059
5	LOTUS DEVELOPMENT CORPORATION/IBM	COMPUTER SOFTWARE	1,558
6	FEDERAL GOVERNMENT	GOVERNMENT	1,464
7	CAMBRIDGE PUBLIC HEALTH COMMISSION	MEDICAL	1,370
8	MILLENNIUM	BIOTECHNOLOGY/R&D	1,211

	PHARMACEUTICALS		
9	COMMONWEALTH OF MASSACHUSETTS	GOVERNMENT	1,124
10	DRAPER LABORATORY	RESEARCH and DEVELOPMENT	1,044
11	BIOGEN	BIOTECHNOLOGY	998
12	ARTHUR D. LITTLE, INC.	MANAGEMENT CONSULTING	887
13	GENZYME	PHARMACEUTICAL PRODUCTS	877
14	QUEST DIAGNOSTICS	CLINICAL TESTING SERVICES	735
15	GENUITY/Formerly GTE INTERNETWORKING	RESEARCH and DEVELOPMENT	731
16	CAMP, DRESSER and MCKEE	ENGINEERING	665
17	SAPIENT CORPORATION	MANAGEMENT CONSULTANTS	641
18	NECCO/HAVILAND	CONFECTIONERY PRODUCTS	622
19	EF EDUCATION	TRAVEL and EXCHANGE PROGRAMS	582
20	GENETICS INSTITUTE	BIOTECHNOLOGY	557
21	WHITEHEAD INSTITUTE	RESEARCH and DEVELOPMENT	550
22	LESLEY UNIVERSITY	EDUCATION	546
23	MODERN CONTINENTAL	CONSTRUCTION	537
24	FORRESTER RESEARCH	BUSINESS SERVICES	483
25	YOUVILLE HOSPITAL	MEDICAL	478
TOTAL			37,880

Top 25 Cambridge Employers: 2006

RANK	NAME OF EMPLOYER	NATURE OF BUSINESS	EMPLOYEES
1	HARVARD UNIVERSITY	HIGHER EDUCATION	10,068
2	MASSACHUSETTS INSTITUTE OF TECHNOLOGY	HIGHER EDUCATION	7,864

3	CITY OF CAMBRIDGE	GOVERNMENT	2,819
4	MT. AUBURN HOSPITAL	MEDICAL	1,813
5	CAMBRIDGE HEALTH ALLIANCE	MEDICAL	1,567
6	FEDERAL GOVERNMENT	GOVERNMENT	1,514
7	BIOGEN IDEC	BIOTECHNOLOGY	1,434
8	GENZYME CORPORATION	BIOTECHNOLOGY	1,370
9	NOVARTIS INSTITUTE FOR BIOMEDICAL RESEARCH	BIOTECHNOLOGY	1,200
10	MILLENNIUM PHARMACEUTICALS	BIOTECHNOLOGY	1,175
11	DRAPER LABORATORY	RESEARCH & DEVELOPMENT	1,061
12	COMMONWEALTH OF MASSACHUSETTS	GOVERNMENT	933
13	VERTEX PHARMACEUTICALS	BIOTECHNOLOGY	836
14	WYETH CAMBRIDGE	BIOTECHNOLOGY	704
15	EF INTERNATIONAL	TRAVEL & EXCHANGE PROGRAMS	685
16	CAMP, DRESSER, and MCKEE	ENGINEERING CONSULTANTS	682
17	WHOLE FOODS	RETAIL SUPERMARKET	593
18	QUEST DIAGNOSTICS	CLINICAL TESTING SERVICES	570
19	LESLEY UNIVERSITY	HIGHER EDUCATION	551
20	SHIRE PHARMACEUTICALS	BIOTECHNOLOGY	475
21	YOUVILLE HOSPITAL & REHABILITATION CENTER	MEDICAL	463
22	MONITOR GROUP	MANAGEMENT CONSULTING	455
23	FORRESTER RESEARCH	BUSINESS SERVICES	444
24	AKAMAI	INTERNET NETWORK SERVICES	417
25	ABT ASSOCIATES	CONSULTING	411

TOTAL			40,515

Since 1995, biotechnology in Cambridge has grown considerably as only 2 of the top 25 employers were biotechnology firms and they employed only 913 people. By 2000, 6 of the top 25 employers were biotechnology firms and the number of people they employed had risen by 450% to 3928. Finally, in 2006, 8 of the top 25 employers were biotechnology companies and the number of people they employed has almost doubled to 7764 people. In little over a decade, biotechnology has emerged as the dominant non-academic employer in the City of Cambridge. Below is a geographical distribution of the top biotechnology employers in Cambridge:

Top Biotechnology Employers in Cambridge

This geographic distribution of the major biotechnology employers in Cambridge demonstrates that most of them are located around MIT. As shall be demonstrated, the

reasons for this locational distribution are a function not only of the scientific attractiveness and technological spillovers that accrue to firms close to MIT but also due to the physical attributes of the buildings in the MIT area.

In 2003, the Massachusetts biotechnology industry which is anchored in the Boston-Cambridge metropolitan area had a substantial economic development impact as it directly employed more than 50,100 people—21.4 directly and 28.7 indirectly—and generated $2.9 billion in earnings and $273 million in state and local taxes.[203] The area is home to notable companies such as Biogen, IDEC, Millennium, Novartis and Genzyme. Since 1993, Boston-Cambridge area employment in pharmaceutical and medicine manufacturing has increased from 3,500 to 8,500 a 143% increase.[204] The figure since 1983 when employment in this sector was only 2,000 represents a 325% increase to the year 2003.[205] However, employment growth in R&D has been particularly explosive. Since 1993, employment in life sciences R&D has grown from 7,300 to 12,800, a 75% increase; and since 1983 when R&D employment was only 3,200, the rate of growth is 300%.[206] While employment growth in both manufacturing and R&D is comparable, the 50% greater aggregate employment in life sciences R&D is indicative of the role of the region's major research universities—Harvard, MIT, Tufts, etc.—as hubs for academic, government and increasingly industry sponsored biopharmaceutical R&D. It also indicates that the labor market in the area is geared more towards highly educated professionals who have the skills necessary to contribute to the biopharmaceutical research milieu.

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[203] United States Department of Commerce 2003: *A Survey of the Use of Biotechnology in U.S. Industry*, Technology Administration and Bureau of Labor Statistics, BEA, Economy.com, Milken Institute.
[204] Ibid.
[205] Ibid.
[206] Ibid.

In view of the significance of this biotechnology cluster, below are some key events in its evolution in Cambridge, Massachusetts:

Key Events in the Evolution of the Cambridge, MA Biotechnology Industry

1981—Genzyme, world's third largest biotechnology company established in Cambridge

1982--Whitehead Institute for Biomedical Research established in Cambridge. Whitehead is a leading, nonprofit research and educational institution that has defined the cutting edge of biomedical science, creating a legacy of research excellence and academic eminence since 1982. Wholly independent in its governance, finances and research programs, Whitehead shares a teaching affiliation with Massachusetts Institute of Technology (MIT), offering the intellectual, collegial and scientific benefits of a leading research university.

1983—Passage of Orphan Drug Act

1985—Establishment of the Massachusetts Biotechnology Council, a not-for-profit organization that provides services and support for the Massachusetts biotechnology industry.

1987—Alkermes, a biotech firm that focuses on drug delivery technologies including "long-acting" or "extended release" formulations of injectable and inhaled drugs, established in Cambridge by MIT trained scientists Michael Wall (electrical engineering), and Paul Schimmel and Alexander Rich (both molecular biology) and Floyd Bloom, a Scripps neuroscientist.

1989—Vertex Pharmaceuticals founded in Cambridge

1990—Whitehead Institute/MIT Center for Genome Research founded, and it becomes an international leader in the field of genomics and a flagship of the Human Genome Project.

1993—Millennium Pharmaceuticals established in Cambridge

1997—Pitkin Petition filed in Cambridge to address concerns with overdevelopment and gentrification in East Cambridge and to promote more affordable housing in the area. It led to an 18 month moratorium on development in excess of 20,000 square feet in the area.

1998—Harvard Medical School-based scientists establish the Institute of Chemistry and Cell Biology to facilitate the pursuit of chemical genetics as an academic discipline.

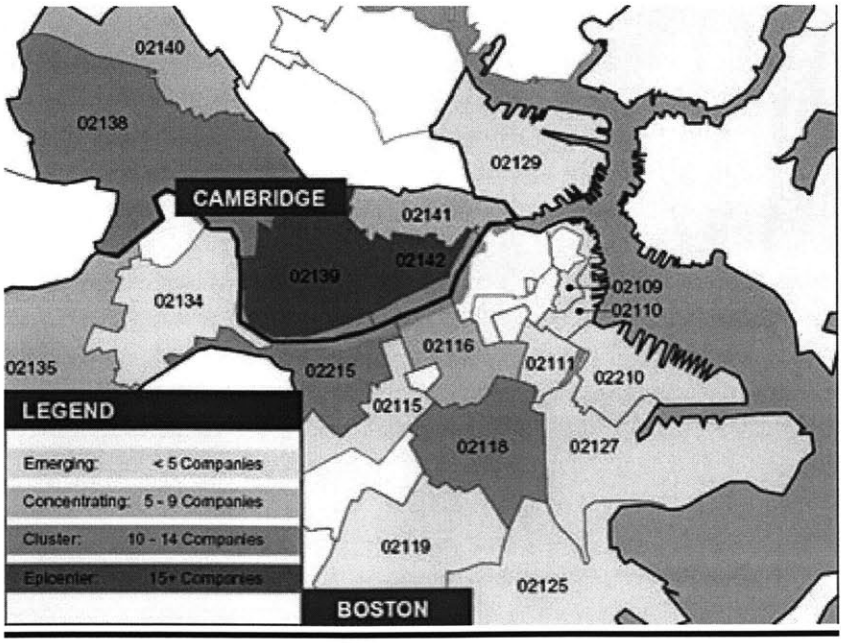
2002—Swiss drug-maker Novartis to lease 764,000 square feet of lab space in Cambridge and invests $750 million to develop, equip, and staff the Novartis Institute of Biomedical Research, the lead research facility and global command center for the company's R&D efforts.

2003--Biogen Idec Inc., a biotechnology company specializing in drugs for neurology, autoimmune disorders, and cancer, formed by the merger of Cambridge-based Biogen and San Diego-based Idec Pharmaceuticals. Biogen Idec is headquartered in Kendall Square in Cambridge, Massachusetts, and operates R&D and manufacturing facilities in Cambridge and San Diego.

2003—Genzyme Center, the company's new headquarters, opens a new headquarters in Cambridge.

2006—Opening of Broad Institute, a research collaboration in genomic medicine involving faculty, professional staff and students from throughout the MIT and Harvard academic and medical communities that is governed jointly by the two universities.

According to the Massachusetts Biotechnology Council, as of 2004, there were 146 life sciences companies in Boston and Cambridge. 64% (93 companies) of the 146 are located in 3 zip codes--02139 (Central Square/MIT), 02142 (Kendall Square/MIT) and 02138 (Harvard Square):[207]



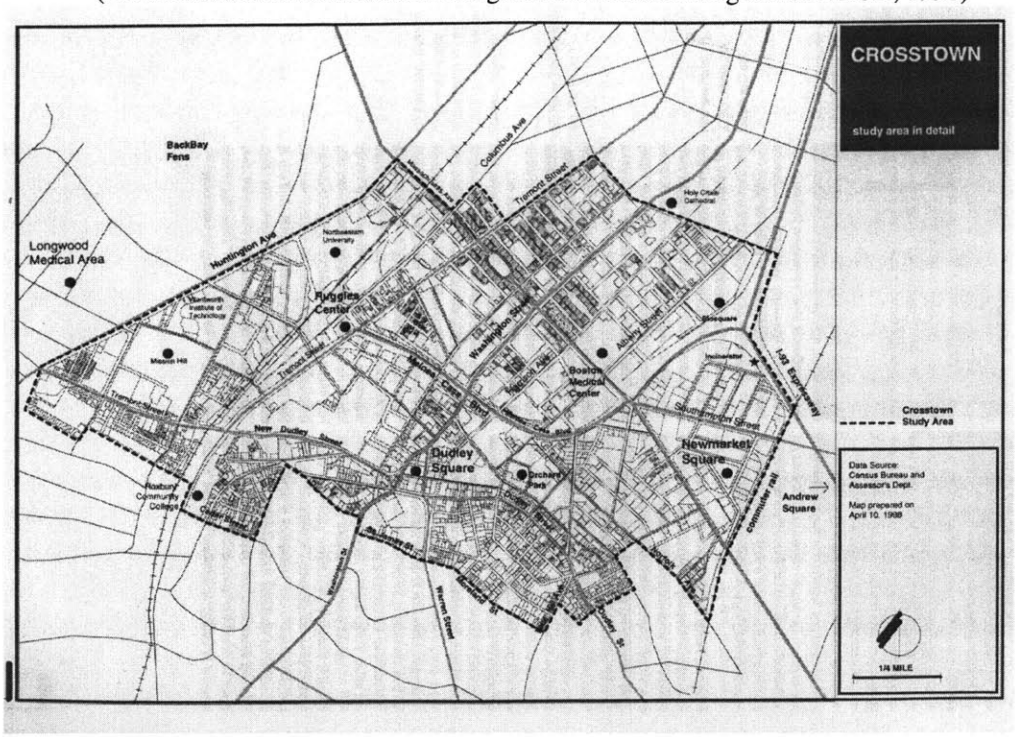
[207] "Early Findings of Mass Impact Study." MIT News Office, August 11, 2004. This figure has since declined to 88 according to the Massachusetts Biotechnology Council's Industry Directory.

More than 50 of these companies are located in the 02139 region (near MIT) alone.[208] 51% of the private life sciences companies in business in July 2004 were started after 2000.[209] 55% of the public life sciences companies in Boston and Cambridge have their headquarters in one of these cities.[210] The others have offices, labs or other ancillary operations at these locations. The revenue of these public companies has grown by almost 60% between 2001 and 2003, from almost $2 billion to more than $3.1 billion.[211] Approximately 10,000 employees work for those public life sciences companies with headquarters in Boston or Cambridge; and an additional estimated 2,200 are employed by public life science companies with other (non-HQ) offices in Boston or Cambridge.[212] Overall, within a mile of MIT, are located 13 of the 25 largest biotechnology companies in Massachusetts.[213]

Likewise Boston is a center for biotechnology, particularly in an area known as Roxbury's Crosstown. Strategically, this area (see map) is ideally located for biotechnology in that it is geographically at the center of the city:

[208] Ibid.
[209] Ibid.
[210] Ibid.
[211] Ibid.
[212] Ibid.
[213] Charles Pierce. "Boston's Biotech Moment." *Boston Globe*, December 14, 2003.

Source: *Crosstown—Enigma or Economic Engine?*
(A Publication of the South End Neighborhood Action Program of ABCD, 1998)



Components of the Biotechnology Cluster

There are several elements and numerous stakeholders in the biotechnology cluster in Cambridge. Aside from the different types of biotechnology companies that are focused on drug production—8 percent of the world's pipeline of new medications are now located in Massachusetts[214]—there is an emerging group of industrial/environmental biotechnology firms whose growth has been catalyzed by MIT's new commitment to addressing the global energy crisis. Even more important is the fact that in Cambridge there a unique mix of firms at different stages of development: well-established global firms alongside small entrepreneurial startups. To establish why these firms have chosen to locate in Cambridge will require an analysis of how these two types of firms—large

[214] MassBiotech 2010 Report. Massachusetts Biotechnology Council, 2002.

and small—interact with public institutions and non-profit/educational institutions that often receive significant public largesse.

According to the 2006 Massachusetts Biotechnology Council's Industry Directory,[215] there are currently 88 biotechnology firms in Cambridge. They are categorized as follows[216]:

	Agricultural Biotechnology	Bioinformatics Services	Biological Devices	Contract Manufacturing	Contract Research	Genomics/ Proteomics	Human Diagnostics	Human Therapeutics	Other
Total	4	4	5	2	5	14	6	56	14

By far the largest group is human therapeutics which is part of the medical biotechnology/biopharmaceuticals industry. Detailed information—derived from the Massachusetts Biotechnology Council's Industry Directory—about these firms is found in the Appendix. For the purposes of this study, biotechnology firms and organizations have been placed in four categories: small firms (less than 5 employees); mid-sized firms (5-50 employees); large firms (greater than 50 employees); and research institutes. Research institutes have been categorized according to size so there is some overlap. My analysis also details the establishment date of the operation. So as to focus on those firms that have demonstrated viability, interviews will be conducted with various biotech community stakeholders from government, academia, mid-sized and large firms, and non-governmental organizations.

[215] http://massbio.org/directory/companies/results.php3?keywords=&city=cambridge&emps=&s=41
[216] Some firms fit into multiple categories.

Categorization of Biotechnology Stakeholders

Small (Less than 5 employees)	**Medium** (5-50 employees)	**Large** (Greater than 50 employees)	**Research Institutes**
Absolute Science	ActivBiotics	Acambis	Broad Institute
Acceleron Pharma	Advanced	Alkermes	Organon Research
Alynylam	Magnetics	Altus	Center
Pharmaceuticals	Alantos	Pharmaceuticals	Novartis Institutes
Cell NetwoRx	Pharmaceuticals	Amgen	for BioMedical
Codon Devices	Archemix	Ariad	Research
Correlagen	Bionaut	Pharmaceuticals	Pfizer Research
FoldRx	Pharmaceuticals	Aveo	Technology Center
Genfit Corporation	BioTrove	Pharmaceuticals	Sanofi Aventis
Gloucester	Boston Biochem	Biogen Idec	Pharmaceutics
Pharmaceuticals	CombinatoRx	Biopure	Cambridge
Keel	Domantis	Curis	Genomics Center
Pharmaceuticals	Elixir	Dyax	Schering-Plough
Link Medicine	Pharmaceuticals	Genzyme	Research Institute
Corporation	Ensemble Discovery	Corporation	Whitehead Institute
Magen BioSciences	Corporation	ImmunoGen	Wyeth Research
Mersana	EnVivo	Infinity	Headquarters
Therapeutics	Pharmaceuticals	Pharmaceuticals	
Oxxon Therapeutics	Etex Corporation	Microbia, Inc.	
Pulmatrix, Inc.	Galenea	Millennium	
Sirtris	Genetix	Pharmaceuticals	
Pharmaceuticals	Pharmaceuticals	Novartis Institutes	
	Gwathmey Inc.	for BioMedical	
	Hydra Biosciences	Research	
	Idenix	Pfizer Research	
	Pharmaceuticals	Technology Center	
	Idera	Sanofi Aventis	
	Pharmaceuticals	Pharmaceutics,	
	Javelin	Cambridge	
	Pharmaceuticals	Genomics Center	
	Kard Scientific	Schering-Plough	
	Merrimack	Research Institute	
	Pharmaceuticals	Shire	
	Metabolix, Inc.	Pharmaceuticals	
	Modular Genetics	Therion Biologics	
	Molecular Insight	Corp.	
	Pharmaceuticals	TolerRx, Inc.	
	Momenta	Vertex	
	Pharmaceuticals	Pharmaceuticals	
	NovoBiotic	ViaCell, Inc.	
	Pharmaceuticals	Wyeth Research	

	OmniGene Bioproducts One Cell Systems Organon Research Center Peptimmune, Inc. Percivia Pervasis Therapeutics Phylonix Pharmaceuticals Radius Saoirse Corporation SolMap Pharmaceuticals Tepha, Inc. WMR Biomedical, Inc. Xanthus Pharmaceuticals	Headquarters	

ESTABLISHMENT DATE

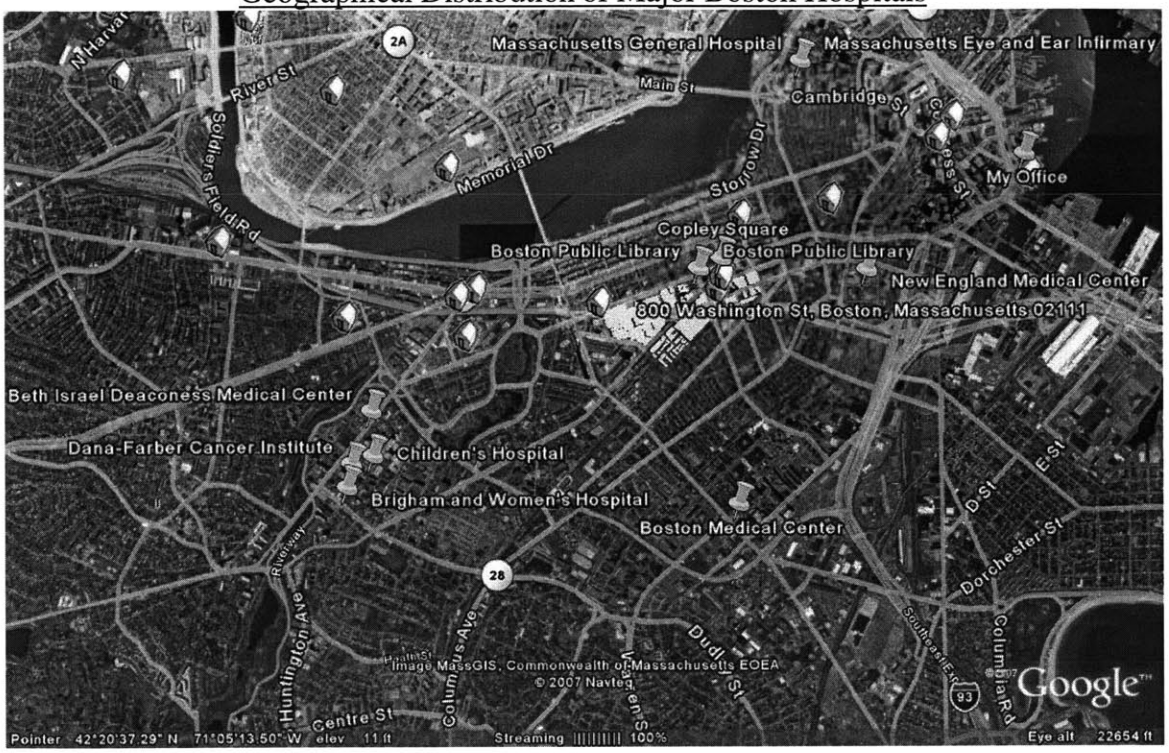
1978: Biogen Idec
1980: Amgen
Wyeth Research Headquarters
1981: Advanced Magnetics
Genzyme Corporation
ImmunoGen
1984: Biopure
1987: Alkermes
1989: Etex Corporation
Idera Pharmaceuticals
Vertex Pharmaceuticals
1990: Acambis
1991: Ariad Pharmaceuticals
Therion Biologics Corp.
1992: Altus Pharmaceuticals
Genetix Pharmaceuticals
One Cell Systems
1993: Metabolix, Inc.
Millennium Pharmaceuticals
1995: Dyax
OmniGene Bioproducts
1996: ActivBiotics
Gwathmey Inc.

TransMolecular
1997: Boston Biochem
Molecular Insight Pharmaceuticals
Phylonix Pharmaceuticals
Shire Pharmaceuticals
1998: Idenix Pharmaceuticals
Microbia, Inc.
Tepha, Inc.
1999: Absolute Science
Alantos Pharmaceuticals
ALS Therapy Development Foundation
Elixir Pharmaceuticals
Genfit Corporation
Pfizer ResearchTechnology Center
2000: Archemix
Bionaut Pharmaceuticals
BioTrove
CombinatoRx
Curis
Merrimack Pharmaceuticals
Modular Genetics
Sanofi Aventis Pharmaceuticals, Cambridge Genomics Center
TolerRx, Inc.
ViaCell, Inc.
2001: Domantis
EnVivo Pharmaceuticals
Genetics Services
Genstruct
Hydra Biosciences
Infinity Pharmaceuticals
Xanthus Pharmaceuticals
2002: Alnylam Pharmaceuticals
Aveo Pharmaceuticals
Kard Scientific
Keel Pharmaceuticals
Momenta Pharmaceuticals
Novartis Institutes for BioMedical Research
Saoirse Corporation
2003: Acceleron Pharma
FoldRx
Gloucester Pharmaceuticals
Peptimmune, Inc.
Pervasis Therapeutics
Pulmatrix, Inc.
2004: Cell NetwoRx
Codon Devices

Galenea
Oxxon Therapeutics
Sirtris Pharmaceuticals
2005: Javelin Pharmaceuticals
Link Medicine Corporation
Organon Research Center
SolMap Pharmaceuticals
WMR Biomedical, Inc.
2006: Magen BioSciences
Schering-Plough Research Institute

Finally, Boston's hospital infrastructure which is in close proximity to Cambridge is a critical component of the biotechnology cluster as it is there that many of the clinical trials that are a vital part of the value chain are conducted. Moreover, the hospitals themselves conduct research, serve as training grounds for area medical school students, and the doctors who work in the hospitals often also serve on company boards. Included within this hospital network are the Boston Medical Center, Brigham and Women's Hospital, Children's Hospital, Tufts New England Medical Center, the Massachusetts Eye and Ear Infirmary, Dana-Farber Cancer Institute, Beth Israel Deaconess Medical Center, and Massachusetts General Hospital—all in such close proximity that collectively they comprise a hospital cluster with Harvard Medical School at the core. Both Beth Israel and Massachusetts General Hospital are teaching hospitals of Harvard Medical School which promotes close ties with Harvard University and the Cambridge community. As the below map shows, these hospitals are not only in the same city but are clustered together in very close proximity which promotes the physical interaction and cultivation of social capital that is crucial to innovation.

Geographical Distribution of Major Boston Hospitals



The quality of the work at these hospitals is evidenced in their consistently high rankings in a U.S. News and World Report survey of 5,189 American hospitals:[217]

Boston Hospitals' National Rankings

Hospital	Rankings
Beth Israel Deaconess Medical Center	#12 Endocrinology #18 Digestive Disorders #32 Respiratory Disorders #42 Heart and Heart Surgery #43 Cancer #47 Kidney Disease
Brigham and Women's Hospital	#2 Gynecology #5 Heart and Heart Surgery #5 Rheumatology #6 Kidney Disease #9 Endocrinology #10 Digestive Disorders #13 Neurology and Neurosurgery #14 Respiratory Disorders #17 Orthopedics #19 Urology

[217] http://www.usnews.com/usnews/health/best-hospitals/tophosp.htm

	#27 Cancer #48 Ear, Nose and Throat
Children's Hospital	#2 Pediatrics
Dana-Farber Cancer Institute	#5 Cancer
Massachusetts Eye and Ear Infirmary	#3 Ear, Nose and Throat #4 Ophthalmology
Massachusetts General Hospital	#1 Psychiatry #2 Endocrinology #3 Neurology and Neurosurgery #3 Orthopedics #4 Digestive Disorders #4 Heart and Heart Surgery #4 Kidney Disease #4 Respiratory Disorders #6 Gynecology #8 Rheumatology #9 Urology #15 Cancer #21 Pediatrics

Indeed, the Boston metropolitan area has organically emerged as a biotechnology center in part because of these hospitals' success in obtaining federal funding for precommercial medical research. They are major centers of biotechnology R&D. Boston alone received $1.1 billion in National Institutes of Health grant funding in fiscal year 2000.[218] If Boston were a state it would be ranked 19th in the nation based upon the NIH funding it receives.[219] $668 million or 62% of this NIH funding was directed to the city's hospitals and medical research facilities.[220] Some of the R&D activities in Boston's medical sector involve research into disease prevention, medical procedures, drug trials, and genetic studies.[221] Indeed, a full 25% of the jobs at Massachusetts General Hospital (a Harvard Medical School teaching hospital) are due to medical research.[222] The following

[218] Sarah Schweitzer. "Vision of Biotechnology Corridor Lacks Allure in Boston Neighborhood," The Boston Globe, March 18, 2002.
[219] Federal R&D Funding in Boston, Boston Redevelopment Authority, May 2002, p.23.
[220] Ibid, p.3.
[221] Ibid, p.14.
[222] Ibid, p.25.

tables delineate how NIH funds were distributed to finance precommercial medical research, an important part of the biotechnology development process:

Total Federal R&D Funding for Boston's Medical Institutions in FY 2000[223]

Institution	Total Funding
Massachusetts General Hospital	$159,807,786
Brigham and Women's Hospital	$151,046,608
Beth Israel Deaconess	$75,336,719
Dana Farber Cancer Institute	$68,231,401
Children's Hospital Boston	$48,609,716
New England Medical Center	$25,640,070
VA Medical Center	$22,213,924
General Hospital Corporation	$21,880,473
Boston Medical Center	$18,373,400
Center for Blood Research	$17,633,231
Joslin Diabetes Research	$14,150,847
Other	$44,370,253
All Medical Institutions	$668,294,428

Top Academic Institutions in Boston Receiving Federal (NIH) R&D Funding in FY2000[224]

Institution	Total Funding
Harvard University (refers to Harvard Medical School, School of Public Health and School of Dentistry located in Boston	$187,331,132
Boston University	$133,843,780
Tufts University (refers to Tufts School of Medicine, School of Veterinary Medicine, and other Tufts facilities located in Boston)	$37,455,771
Northeastern University	$22,204,632
Boston College	$3,469,771
UMASS Boston	$2,364,999
New England College of Optometry	$1,087,596
Simmons College	$552,859
Wentworth Institute of Technology	$406,000
All Academic Institutions	$388,716,540

These figures do not account for the funding that MIT and Harvard and Tufts affiliated institutions such as the MIT-Whitehead Institute which are located in Cambridge and other localities receive.

[223] Ibid, p.15.
[224] Ibid, p.16.

Using the Regional Economic Models, Inc. (REMI) econometric model, the economic impact of the 1.1 billion in NIH funding available for R&D research upon jobs created and dollar additions to the Gross Regional Product, has been calculated as:

Economic Impact of Federal R&D Spending in Boston[225]

Impact	Boston
Number of Jobs Created	18,030
Gross Regional Product Created	$842,252,800

Due in significant part to these federal funds, and the success of the city's hospital network in attracting them, Boston's health services sector represents more than one out of six city jobs, with 103,835 people employed in 2003, including all employment in Boston's 22 inpatient hospitals, 25 community health centers, nursing homes and community, family, and child services.[226]

Over the past five years, federal grants to teaching hospitals in Boston have doubled to $1.4 billion annually as of 2005.[227] Medical institutions in the Boston area employ more than 150,000 workers and added over $24 billion to the state's economy in 2005.[228] The top 15 largest NIH grantees in Massachusetts are as follows:

[225]Ibid, p.21.
[226] http://www.tbf.org/indicators2004/economy/overview.asp
[227] Super Cluster. 2007. A joint publication of the Massachusetts Technology Collaborative, PriceWaterhouseCoopers and the New England Healthcare Initiative.
[228]Ibid.

15 Largest NIH Grantee Institutions in Massachusetts, 2005[229]

Rank	Organization	Dollars Award ($ millions)
1	Massachusetts General Hospital	$287
2	Brigham and Women's Hospital	$253
3	Massachusetts Institute of Technology	$172
4	Harvard University Medical School	$169
5	Boston University Medical Campus	$123
6	Beth Israel Deaconess Medical Center	$123
7	Dana-Farber Cancer Institute	$117
8	University of Massachusetts Medical School	$115
9	Children's Hospital Boston	$103
10	Harvard University (School of Public Health)	$102
11	Tufts University Boston	$75
12	Harvard University	$51
13	New England Medical Center Hospitals	$50
14	Boston Medical Center	$39
15	Whitehead Institute for Biomedical Research	$35

[229] Ibid.

Summary

The importance of Boston's hospital network is critical to the vitality of the biotechnology cluster in Cambridge. Given that testing, which can take years of refinement, is an essential part of the biotechnology value chain, the hospital network plays a key role in transforming the scientific innovations that emerge from the Cambridge scientific community into real, practical products. More importantly, the attractiveness of the hospital network, which is continually highlighted in the interviews below, demonstrates that Cambridge's talent alone is not the only driving factor behind the locational decisions of those firms that elect to reside and remain in Cambridge. Rather, the benefits of Boston's hospitals which include access to federally financed innovations at hospitals, a powerful network of medical practitioners and the social capital intrinsic to such, and the importance that testing plays for products that have life or death impacts on human beings are all part of why firms locate in Cambridge.

Part IX: Case Studies of Biotechnology Firms in Cambridge

In this section, I will delineate case studies of several of the key biopharmaceutical firms whose locational decisions have been analyzed in this dissertation. I will describe their overall economic and commercial position and present their own assessment of the factors that influence their specific locational decisions. This information will inform subsequent conclusions and provide a factual basis for assessing my hypothesis that the success of Cambridge in attracting biotechnology firms to locate in its biotechnology cluster is the outcome of a distinct set of local, state and federal government policy choices that have catalyzed the development of the biopharmaceutical industry. The specific companies to be analyzed are Genzyme, Pfizer, Bristol-Myers Squibb, Idera Pharmaceuticals, and Ensemble Discovery Corporation. The locational distribution of these company facilities and a geographic description of the broader area is evident in this map:

Geographical Distribution of Case Studies

This map shows that the geographical distribution of these companies is centered around MIT not Harvard. However, Genzyme does have a facility in Allston, a Boston area in which Harvard University has substantial real estate holdings. The locational distribution reflects, in part, the geographical distribution of old factory-type buildings with high ceilings and reinforced floors that biotechnology firms value and have renovated over the past two decades.[230] Such space is not located in Harvard Square, which is densely populated and well-developed, but rather is abundant in the environs of MIT, which has only recently experienced a building boom of its own. Until the recent renovation of Kendall Square, many of the buildings around MIT were of non-descript factory quality and even now, both the infrastructure in and physical area around Central Square is relatively underdeveloped.

[230] Interview, January 30, 2007.

Genzyme

Genzyme, which is headquartered in Cambridge, is one of the world's largest biotechnology companies. Founded in 1981 by a small group of scientists including Charles Cooney of MIT, the company has grown into a diversified corporation with $3.2 billion in revenues and over 9,000 employees.[231] These personnel are spread across 75 locations including 15 manufacturing facilities and 9 genetic testing laboratories in 32 countries.[232] Genzyme is a pure biotechnology company. It was not started prior to the molecular biology revolution of the 1980s but is rather a product of that surge in scientific innovation. As such it is deeply embedded in the DNA of the Cambridge biotechnology industry. Locationally, its challenge has not been to move to the Cambridge biotechnology cluster so as to learn about an emerging science but rather to manage its growth within Cambridge as it seeks to remain anchored in the region that gave birth to the company. Genzyme's growth and distribution of facilities illustrates the gradual regionalization of the biotechnology cluster in Massachusetts. Today, the company has offices and plants in Cambridge, Allston, Framingham, Waltham and Westborough.

Genzyme specializes in developing and commercializing orphan drugs—those that target rare diseases affecting fewer than 200,000 people in the United States and as such are entitled to tax breaks and market exclusivity because they are covered by the federal Orphan Drug Act of 1983. Genzyme is focused on six broad areas of medicine including lysosomal storage disorders, renal disease, orthopedics, transplant and immune

[231] http://www.genzyme.com/corp/structure/fastfacts.asp
[232] http://en.wikipedia.org/wiki/Genzyme

diseases, diagnostics, and oncology.[233] Lysosomal storage disorders are inherited diseases that typically affect fewer than 10,000 people worldwide and are caused by enzyme deficiencies.[234] Genzyme's key products in this area are Cerezyme for Type 1 Gaucher disease, and Fabrazyme for Fabry disease. The renal division develops, manufactures and distributes products that treat patients suffering from renal diseases, including chronic renal failure.[235] Genzyme's major product in this area is Renagal, a calcium-free, metal-free phosphate binder that reduces phosphorous levels in patients with end-stage renal disease. Orthopedics develops manufactures and develops, manufactures and distributes biotherapeutics and biomaterial products. A notable product herein includes Synvisc, which is one of the world's top therapies to treat the pain of osteoarthritis of the knee. In the transplant and immune diseases space, Genzyme develops, manufactures and distributes therapeutic products that address pre-transplantation, prevention and treatment of acute rejection in organ transplantation.[236] Its major product in this area is Thymoglobulin, which treats acute rejection in kidney transplant patients by suppressing the body's natural immune response.[237] Diagnostics provides testing services for the cancer, prenatal and reproductive markets.[238] The company is moving toward personalized medical solutions by developing tests that can help physicians identify how patients are likely to respond to targeted therapies.[239] Finally, in the oncology/blood disease realm, Genzyme has three major drugs: Campath and Clolar for leukemia; and

[233] http://www.genzyme.com/corp/structure/corporateoverview.asp
[234] Ibid.
[235] http://finance.google.com/finance?q=GENZ
[236] http://finance.google.com/finance?q=GENZ
[237] http://www.genzyme.com/corp/structure/corporateoverview.asp
[238] http://finance.google.com/finance?q=GENZ
[239] http://www.genzyme.com/corp/structure/corporateoverview.asp

Thyrogen, for thyroid cancer.[240] As of fiscal year 2006, the company's most profitable products were Cerezyme ($1 billion in revenues), Renagal ($515 million in revenues), Fabrazyme ($359 million in revenues), and Synvisc ($234 million in revenues).[241] Cerezyme has a profit margin set at 60%.[242]

Since both Cerezyme and Fabrazyme, which generate $1.359 billion of the company's $3.2 billion in 2006 revenue, are covered by the Orphan Drug Act, at least 42.5% of the companies revenues are influenced significantly by federal policy. Indeed, the role of the Orphan Drug Act has been crucial to the evolution of Genzyme as from its inception, the company, which has been led by CEO Henri Termeer since 1983, embraced a contrarian strategy of "thinking small" while most large pharmaceutical companies searched for drugs that have a market potential of millions of people.[243] Specifically, at its inception, the company was primarily devoted to finding drugs that would cure enzyme deficiency conditions that were essential to one's survival and which usually afflict a very small percentage of the world's population.[244] Drugs used to treat such conditions are known as "orphan drugs" and in 1983, the US Senate passed legislation creating a category of orphan drugs that treated ailments suffered by fewer than 200,000 patients in the U.S in order to provide incentives for companies to develop them.[245] According to the law, any company that came out with an orphan drug that was approved by the FDA had the right to market that drug exclusively for seven years without facing any competition from a competing drug unless the latter proved to have

[240] http://finance.google.com/finance?q=GENZ
[241] http://www.genzyme.com/corp/structure/fastfacts.asp
[242] http://en.wikipedia.org/wiki/Genzyme
[243] Ibid.
[244] Ibid.
[245] Ibid.

better effects than the one existing in the market.[246] The law also allowed the company that came with an orphan drug for tax deductions equal to half its capital investment in clinical trials.[247] In a costly industry, the protections offered by the federal Orphan Drug Act have therefore been significant to the viability of Genzyme's business model. Moreover, since Genzyme has about 20 key clinical trials underway for new products, access to a strong ecosystem of hospitals is a critical strategic imperative for Genzyme, which impacts its locational decisions.[248] Strategically, the company also partners with other companies to develop new products and supports research conducted by top academic and independent medical science centers so networking opportunities play a role in its locational decisions.[249] Due to the importance that it attaches to the Boston area's hospital network and networking with academic and medical science centers, the company is committed to remaining in the Cambridge metropolitan area.[250]

Genzyme, one of the largest biotechnology companies in the world, is illustrative of the locational dynamics of biotech companies in the Cambridge metropolitan area. It is an example of how the biotechnology industry in the Cambridge metropolitan area has regionalized into several min-clusters with Cambridge as a hub surrounded by the spokes of Waltham, Framingham, etc. The company, which was established in 1981 in an area around Tufts Medical Center that was known as the Combat Zone for its crime and prostitution has evolved from a startup into a company with $3 billion in annual revenues and 9,000 employees. It has made a concerted effort to remain in the Cambridge area despite its expansion and continual need for new space. In 1991, the company moved to 1

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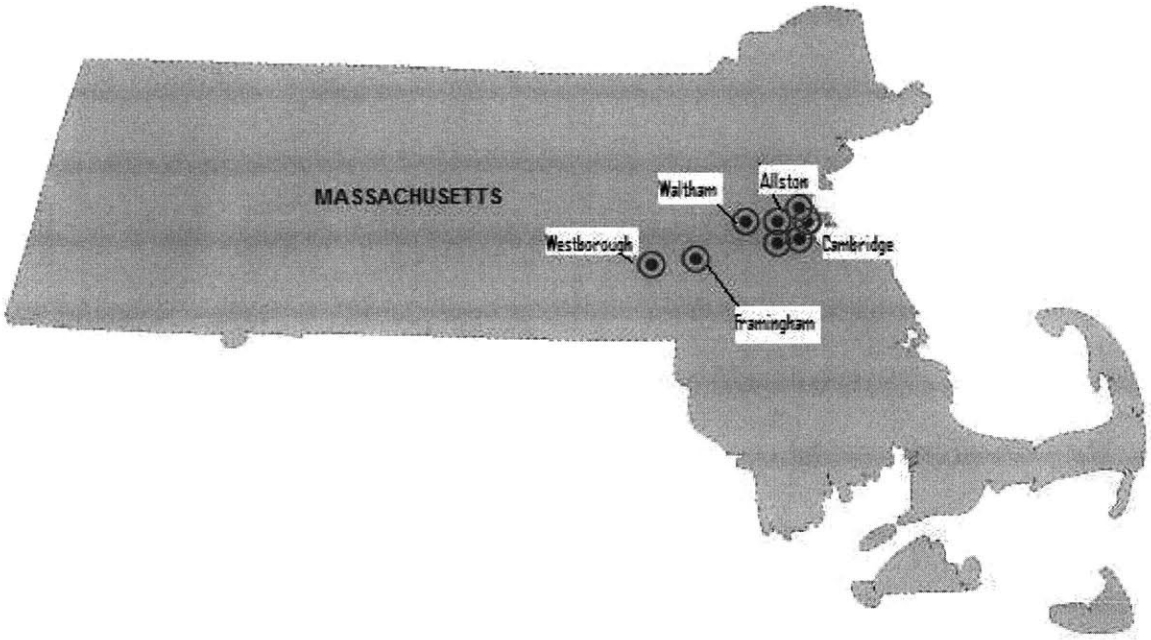
[246] Ibid.
[247] Ibid.
[248] http://www.genzyme.com/corp/structure/corporateoverview.asp
[249] Ibid.
[250] This section is based upon an interview with Elliott Hillback, March 9, 2007.

Kendall Square near MIT and it has since added myriad types of spaces ranging from research and development to a processing facility for packaging on Binnet St. It has also made local acquisitions around University Park Hotel near MIT and the company also has a couple of floors of space along Ed Lam Boulevard. In 1989, it acquired Integrated Genetics in Framingham and that 21 million square feet facility has become its regional headquarters for bioscience manufacturing—in no small part due to its bigger size and cheaper land—while another facility in Waltham, which it obtained when it acquired Geltex in 2000, serves as the center for products that are based on chemistry such as biopolymers. Its genetic testing business is in Westborough and the company has 24/7 biomanufacturing facility of 1.5 million square feet in Allston Landing. The company has recently moved its headquarters to 500 Kendall Street—Genzyme Center—where it has built a "green"/environmentally sound construct to house 900 employees. Unlike Novartis, which uses Cambridge as the global center for its research and development, as Genzyme has evolved, it no longer does a lot of its research and development in Cambridge but rather utilizes its Cambridge operation for business units such as marketing and finance. Cambridge has become a coordinating point for the collaboration amongst various functions that Genzyme requires because the biotechnology industry is so very flexible. This map which is followed by a list of functions at each facility shows the geographical distribution of Genzyme's operations in and around Cambridge:



Geographical Distribution of Genzyme's Facilities in Greater Cambridge Area[251]

Location	Function	Date
Combat Zone Downtown Crossing/Chinatown Boston	Founding Location for Startup	1981
15 Pleasant St. Connector Framingham, MA 01701-9322	Bioscience Manufacturing	Acquired in 1989; renovated and expanded for Fall 2007
One Kendall Square Cambridge,MA 02139-1562	Business Operations	1991
500 Soldiers Field Road Allston, MA 02134	Protein Manufacturing	1996
64 Sidney Street Cambridge, MA 02139	Cell Manufacturing	1997
153 Second Avenue Waltham, MA 02451	Drug Discovery and Development	2000
3400 Computer Drive Westborough, MA 01581	Genzyme Genetics	2002

[251] Based upon interview data with Elliott Hillback and company information at www.genzyme.com

55 Cambridge Parkway Cambridge, MA 02142	Biosurgery	2002
Genzyme Center 500 Kendall Street Cambridge, MA 02142	Corporate Headquarters	2006

All of the different facilities it has established are close enough to facilitate regional coordination. The firm's rapid growth—annual earnings grow between 15-20%--has meant that it has consistently outgrown its space in Cambridge. Although Genzyme would prefer to have 1 big space in Cambridge instead of 6 or 7 buildings, and despite the difficulties of dealing with local governments that have more entrenched power and a greater history of independence, the firm has remained committed to the area because they believe that they need to be physically present so as to interact for innovation. In the view of Genzyme, while there are places like Singapore and Ireland that will bend over backward to help one establish an operation there, the Greater Boston area is a core region that the firm intends to be anchored in despite the cost. According to Mr. Hillback, due to the scale of Genzyme's operations, government policies such as tax increment financing are not a driving factor in his firm's locational decisions. As Mr. Hillback notes: "Taxes matter less than talent. We would not leave over taxes." He cites as an example, the decision to invest in Allston which was the least beneficial financially and most expensive option but which was made in part because of Genzyme's regional approach to its locational strategy and because of a desire to be visible and demonstrate a commitment to remaining in the Cambridge area. For firms like Genzyme, location matters as convenience and interaction are critical since one cannot isolate functions. Hence, the locational decisions of firms—and the attendant influence of government in those decisions—in the Cambridge metropolitan area are influenced by the size of their

operation and their strategic imperatives. A critical exception to this occurred at the state level when Massachusetts considered buying generic drugs from Canada and the biotechnology industry, which was concerned about not being reimbursed for its research and development of intellectual property, mobilized against that proposal which was eventually rejected.

Pfizer

Pfizer Inc., established by German-American cousins Charles Pfizer and Charles Erhardt in Brooklyn, New York in 1849, is now the largest pharmaceutical company in the world. The company discovers, develops, manufactures and markets prescription medicines for humans and animals.[252] Pfizer's original core competency was in chemistry. Government has played a role in the evolution of Pfizer as the company which was known in the first half of the 20th century as an expert in fermentation technology applied those skills during World War II on behalf of a major client—the United States government—to mass produce penicillin to treat injured Allied soldiers.[253] Indeed, most of the penicillin that went ashore with the troops on D-Day was made by Pfizer.[254] At present, Pfizer, which has over 106,000 employees, is organized into three divisions with total 2005 revenues of $51.3 billion: Human Health ($44.28B in 2005 sales), Consumer Healthcare ($3.87B in 2005 sales), Animal Health ($2.2B in 2005 sales), and Corporate Groups (which includes legal, finance, and HR).[255] In December 2006, the company sold its Consumer Healthcare business which included famous brands such as Listerine Nicorette, Visine, Sudafed and Neosporin to Johnson & Johnson for $16.6 billion.

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[252] http://finance.google.com/finance?q=pfizer
[253] http://en.wikipedia.org/wiki/Pfizer
[254] Ibid.
[255] Ibid.

The revolution in molecular biology that catalyzed the biotechnology industry has significantly influenced the company's locational paradigm and business strategy. It has been forced to look outside the company for scientific innovations while its headquarters including core marketing and management staff remain in New York. Consequently, Pfizer has approximately 10 global research and development centers including a Research Technology Center in Cambridge which was established in 1999. The other centers are in Groton and New London, Connecticut; Sandwich, England; Ann Arbor and Kalamazoo, Michigan; St. Louis, Missouri; La Jolla, California; and Nagoya and Tokyo, Japan. These research centers serve as listening posts and early warning systems as to which scientific innovations the company needs to pay close attention. Specifically, the mission of the RTC in Cambridge is to apply the latest technologies to address challenges in health care.[256] The RTC, which employs 100 staff with projected expansion to 150, occupies 97,000 square feet in a research and development facility on Memorial Drive overlooking the Charles River between MIT and Harvard.[257] Its project work focuses on the early stages of the drug discover process including target identification, screening, optimization and chemical tool production.[258]

During the 1980s and 1990s, Pfizer underwent a period of sustained growth driven by the discovery and marketing of multiple successful drugs including Zoloft (for depression), Aricept (for Alzheimers), Zithromax (for bacterial infections), Diflucan (an oral antifungal medication), Norvasc (hypertension), and Viagra (the well-known erectile dysfunction drug).[259] By 2000, it had sales of approximately $10 billion but those

[256] http://www.pfizerrtc.com/about.htm
[257] Ibid.
[258] Ibid.
[259] http://en.wikipedia.org/wiki/Pfizer

increased dramatically to $55 billion in sales when Pfizer merged with Warner-Lambert in 2000 and acquired full rights to Lipitor the number-one selling drug in the world which is used to lower blood cholesterol.[260] In 2002, Pfizer merged with competitor Pharmacia to become the largest pharmaceutical company in the world. The merger was driven in part by the desire to acquire full rights to another product, this time Celebrex, which is used for the treatment of osteoarthritis, adult rheumatoid arthritis, acute pain, menstrual pain and familial adenomatous polyposis.[261] All of this drug development requires considerable expense and in 2005, Pfizer was the industry's largest research and development organization with $7.4 billion in expenditures, an amount equal to approximately four times the budget of MIT.[262]

The federally determined length of patents has a significant impact on corporate decisions with regard to which plants to open, close, and expand. For example, in January 2007, Pfizer announced that it will cut 10,000 jobs and close two manufacturing plants in the United States and sell a third in Germany.[263] This is due to the fact that the market exclusivity afforded by the federal patents for Zithromax and Zoloft has expired which cost Pfizer $2.5 billion in sales in 2006 as revenue declined to $48.3 billion due to an influx of generic drugs.[264] Other drugs scheduled to go off-patent include Norvasc (September 2007). Between 2010 and 2012, drugs representing 41% of Pfizer's sales will come off patent including Aricept, Lipitor, Detrol, and Geodon.[265] However, federal government policy is not the only factor in those decisions. According to Dana Mead, the

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[260] Interview with Dana Mead, March 15, 2007.
[261] http://en.wikipedia.org/wiki/Pfizer
[262] Interview with Dana Mead, March 15, 2007.
[263] http://www.in-pharmatechnologist.com/news/ng.asp?n=73592-pfizer-prudential-equity-group-job-cuts-plant-closure-patent-expiry
[264] Ibid.
[265] Ibid.

Chair of the MIT Corporation, and a board member of Pfizer, the need to network and collaborate plays a role in locational decisions.[266] Collaboration is important at the research level as well as between development and manufacturing people because it is during that process that dosage levels must be determined and it must be decided whether the product will be a capsule, tablet or liquid.[267]

One of the innovative ways that these collaborations occur is through the Cambridge RTC's Drug Pfinder program, which works to bring novel discoveries to Pfizer Global R&D through collaborations with academic groups in the Cambridge community with the ultimate aim of bringing new drugs to market.[268] The intellectual property generated within the program is owned by Pfizer. The Pfinder program is an example of how Pfizer uses the RTCs as listening posts. As part of the program university scientists participate in the early drug discovery process of identifying new chemical leads and are allowed to reap financial benefits if their molecular targets become part of Pfizer's portfolio.[269] However, while academics may benefit if their discoveries make it to market, Pfizer also benefits by deriving knowledge about the direction of scientific inquiry in its field and identifying candidates for recruitment to the firm's research and development labs. Thus, opportunities to network with leading scientists, many of whom have their research funded by NIH and NSF, is a key factor in the locational imperatives of Pfizer.

With regards to Pfizer's locational decisions, access to and retention of talent is a key factor. According to Mr. Mead, a key issue that Pfizer has had to weigh during its

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[266] Interview with Dana Mead, March 15, 2007.
[267] Ibid.
[268] http://drugpfinder.com/mission/mission.htm
[269] Ibid.

recent retrenchment is that one is dealing with great people who are not easily replaced and that may affect your decision.[270] The company may stay with a less effective locational model in the short haul to hold on to its personnel so that it can reap benefits over the long haul. In Pfizer's case, they decided to downsize and focus on research which did not impact the staff in Cambridge since that is what they are focused on. Nonetheless, people issues are key because employees do not move easily when they concentrate labs. Relatedly, a primary factor in Pfizer's locational decisions and personnel is to be in a locale that is attractive to highly qualified people because the quality of life is good, there are good schools, and a good recreational environment including shopping and arts and entertainment. Cambridge meets those criteria but it does place a strain with regards to cost due to the high value of real estate. Indeed, to build a facility in Cambridge of any size, you must spend 25% more (in terms of construction and real estate cost) than in Framingham because one must build a parking garage. This forces factories out. Moreover, Mead points out that the most important element of local infrastructure is not roads but airports and fixed line information and communications technology because these highly talented people employed by Pfizer communicate and travel a lot. At the state level, the biggest issue for a firm like Pfizer is when states entertain the importation of generics which affects the price that companies can competitively charge. Finally, research talent is not the only talent that it is important to have access to. Like Genzyme, Pfizer conducts thousand of clinical trials both locally and nationally so access to Boston's hospital network is highly prized.

[270] This section is based upon an interview with Dana Mead, March 15, 2007.

Bristol-Myers Squibb

Bristol-Myers Squibb is a global pharmaceutical company with $17.9 billion in sales and 43,000 employees.[271] Although Bristol-Myers was founded in 1887 by William McLaren Bristol and John Ripley Myers in Clinton, NY, the present company is the result of a 1989 merger with the Squibb Corporation.[272] The company has three product segments: Pharmaceuticals, Nutritionals and Other Health Care. Its pharmaceutical products fall in different therapeutic classes, such as cardiovascular; virology, including human immunodeficiency virus (HIV); oncology; affective and other (psychiatric) disorders, and immunoscience.[273] The Nutritionals segment consists of Mead Johnson Nutritionals, primarily an infant formula and children's nutritionals business.[274] The Other Health Care segment consists of ConvaTec and Medical Imaging.[275] Pharmaceuticals net sales accounted for 77% of BMS' net sales during the fiscal year ending December 31, 2006. The company's major cardiovascular product is Plavix. The Nutritionals segment, through Mead Johnson, manufactures, markets, distributes and sells infant formulas and other nutritional products, including the entire line of Enfamil products.[276] Nutritionals sales accounted for 13% of the company's sales in 2006.[277] The Other Health Care segment consists of ConvaTec and Medical Imaging. Other Health

[271] http://www.bms.com/aboutbms/data/index.html
[272] http://en.wikipedia.org/wiki/Bristol_Myers_Squibb
[273] http://finance.google.com/finance?q=Bristol-Myers+Squibb&hl=en
[274] Ibid.
[275] Ibid.
[276] Ibid.
[277] Ibid.

Care sales accounted for 10% the company's sales in 2006.[278] ConvaTec manufactures, distributes and sells ostomy, and wound and skincare products.

Bristol-Myers Squibb's, like Pfizer, is headquartered in New York City. The company has major research and development facilities in the New Jersey locales of Princeton, Hopewell, and New Brunswick, as well as Wallingford, Connecticut, Braine-l'Alleud, Belgium and Tokyo, Japan. Four of these six research and development centers are in the Northeast Corridor in easy commuting distance of headquarters in New York City. This highlights a locational focus on keeping innovative activity in close proximity to executive decisionmakers. However, unlike the aforementioned large biopharmaceutical firms, the company does not have a research and development facility in Cambridge. Rather, it has recently chosen to establish a manufacturing facility at a former army base west of Boston.

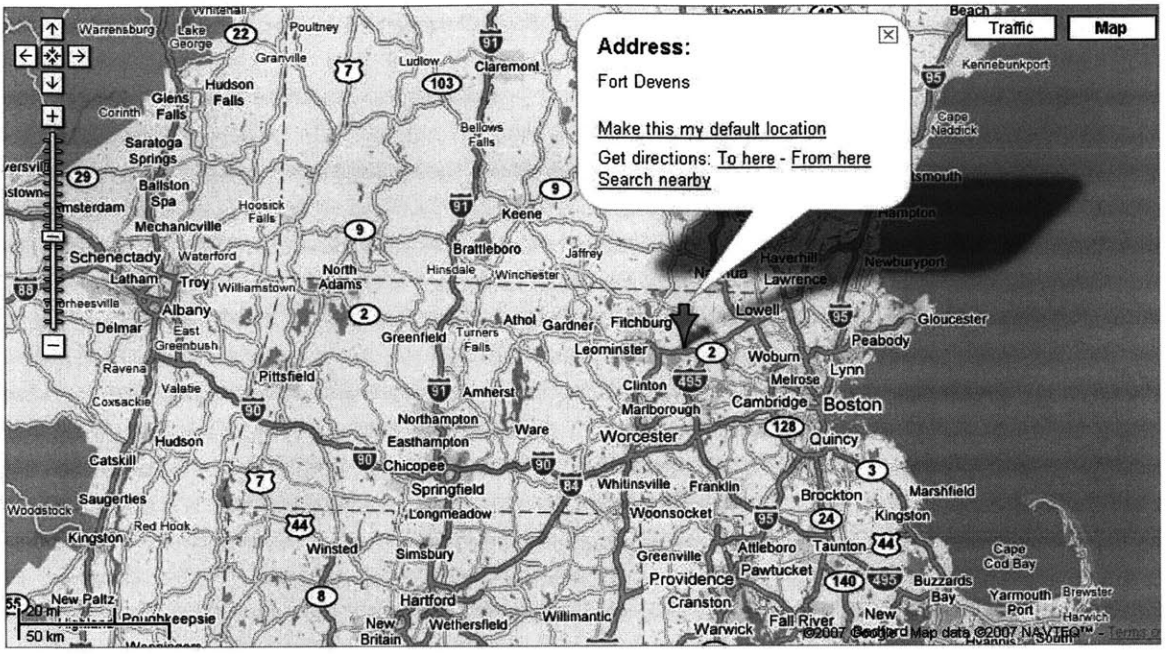
Bristol-Myers Squibb like Pfizer is a pharmaceutical company whose original core competence in chemistry was challenged by the advent of the revolution in molecular biology. It has adapted to this new reality, not by seeking closer ties with the major biotech centers such as Cambridge but rather by its focus on the development of industry alliances. Bristol-Myers Squibb is a company in which greater than 50% of its sales come from products developed through alliances with industry partners such as Adnexus and AstraZeneca.[279] For example, in February 2007, Bristol-Myers Squibb announced that it had entered into a strategic alliance to discover, develop and

[278] Ibid.
[279] http://www.bms.com/alliances/data/index.html

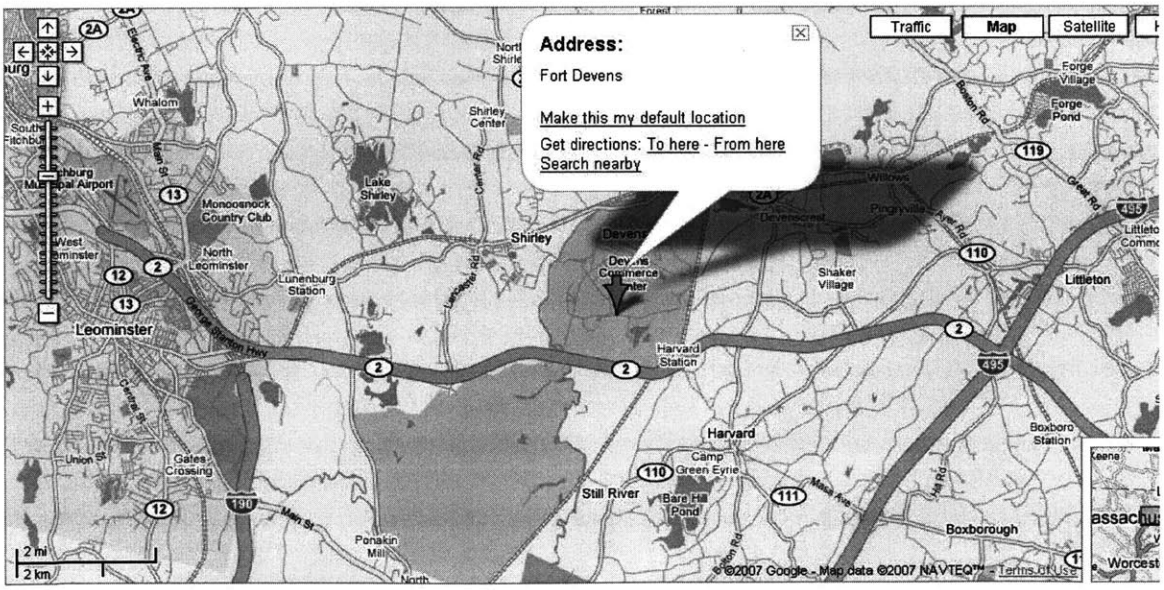
commercialize Adnectin-based therapeutics for oncology-related targets.[280] As part of this agreement, Bristol-Myers Squibb will provide financing of approximately $30 million over three years to Adnexus, consisting of upfront and guaranteed research payments, and it will be responsible for global development and commercialization activities.[281] With regards to the AstraZeneca alliance, it will play a marketing and manufacturing role in the development of drugs for Type 2-diabetes.[282] Through these alliances, Bristol-Myers Squibb is in effect outsourcing its research and development to pure biotech firms so that it can focus on marketing, manufacturing and commercialization. This process which is known as "externalization"[283] reduces the need for Bristol-Myers Squibb to locate in Cambridge to conduct research. Nonetheless, Bristol-Myers Squibb's significance vis a vis this study lies in the dynamics of its decisions to set up a drug manufacturing plant in Fort Devens. As shall be demonstrated this decision was heavily influenced by state government intervention.

[280] http://newsroom.bms.com/index.php?s=press_releases&item=237
[281] Ibid.
[282] http://newsroom.bms.com/index.php?s=press_releases&item=230
[283] http://www.biomarketgroup.com/content/view/80/7/

Fort Devens: Regional Perspective



Fort Devens: Closeup



An example of how state support for infrastructure can be beneficial to inducing firms to locate in Massachusetts is the Bristol-Myers Squibb $660 million deal in June 2006 to construct a new facility to manufacture biologics compounds in Devens,

Massachusetts.[284] The state of Massachusetts--in competition with other southern states such as North Carolina as potential venues for the plant—facilitated Bristol-Myers Squibb's acquisition of 750,000 square feet on 88 acres at the former Fort Devens, an Army base decommissioned in the early 1990s that has been the focus of redevelopment efforts. In order to broker the deal, state officials agreed to commit $34 million for infrastructure to support the plant which is expected to generate at least 350 jobs that pay an average salary of $60,000.[285] The state also agreed to extend investment tax credits.[286]

Idera Pharmaceuticals

Idera Pharmaceuticals, Inc. is a five year old biotechnology startup founded by Sudhir Agrawal and based on his technology that is engaged in the discovery and development of therapeutics that treat immune responses. Its focus is on toll-like receptors (TLRs) for the treatment of multiple diseases including: cancer, infectious diseases, asthma/allergy, autoimmune diseases, and for use in combination with therapeutic and prophylactic vaccines.[287] The company is located in a 26,000 square foot research and development facility on Vassar Street in Cambridge. It has only 27 employees and $2.42 million in revenue.[288] Its leading drug candidate, which is still under development, is IMO-2055, a synthetic DNA-based compound that acts as an agonist for toll-like receptors, and triggers the activation and modulation of the immune system.[289] IMO-2055 is currently in a Phase II clinical trial as a monotherapy for renal

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f[284] See Google Maps.
[285] Mark Jewell. "Bristol-Myers Squibb to build manufacturing plant at Devens." *Boston Globe*, June 1, 2006.
[286] Ibid.
[287] http://finance.google.com/finance?q=IDP
[288] http://www.iderapharma.com/about_idera.php
[289] http://finance.google.com/finance?q=IDP

cell carcinoma and a Phase I/II clinical trial in combination with chemotherapy agents for solid tumors.[290] In May 2005, Idera entered into a research collaboration and option agreement and a license, development and commercialization agreement with Novartis, a Swiss pharmaceutical that is also located in Cambridge, to discover, optimize, develop and commercialize immune modulatory oligonucleotides that are TLR9 agonists, and that are identified as potential treatments for asthma and allergies.[291] It is also collaborating with Merck & Co. for use of specific agonists of TLR9, TLR7 and TLR8 for incorporation into therapeutic and prophylactic vaccines for cancer, infectious diseases and Alzheimer's disease.[292]

According to Robert Anderson, the CFO and VP of Idera, its locational decisions were originally motivated by a desire to be close to the big pharmaceutical firms and other biotech companies in Cambridge.[293] In addition, it was attracted by the fact that the physical character of the space that it occupies in Cambridge was such that it was able to be custom built for Idera's purposes.[294] The company recently considered moving to Arsenal or Worcester, which is 45 miles west of Boston, but decided to remain in Cambridge when its lease expires so as to be close to what is going on in Cambridge and to facilitate close collaborations with Novartis and Merck.[295] Hence for this young startup, networking and the physical character of the buildings in Cambridge and not government policy has been the paramount consideration in its locational decisions.

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[290] Ibid.
[291] Ibid.
[292] Ibid.
[293] Interview with Robert Anderson, March 26, 2007.
[294] Ibid.
[295] Ibid.

Ensemble Discovery Corporation

Ensemble Discovery Corporation is a biotechnology startup that was established in 2003 in partnership with venture capital firm Flagship Ventures to commercialize technology invented by Professor David Liu of Harvard University. This technology known as DNA Programmed Chemistry is a potentially revolutionary approach to controlling chemical synthesis that enables discovery of chemical compounds and chemical reactions on an unprecedented scale by employing DNA to enhance chemical reaction rate and chemical specificity.[296] The company, which is located on Erie Street in Cambridge, has raised $27 million in capital and has 35 employees but no revenues as it is still developing its product.[297] The company also has ties to MIT as Noubar Afeyan, the co-founder and chairman of Flagship Ventures is a graduate of the university and continues to lecture there.

According the Edward Freedman, the company's General Counsel and Vice-President of Operations and Finance, as an early stage life sciences company, Ensemble's locational decisions have been driven by the imperative of being close to both the company's founder, David Liu, and its venture capital partner, Flagship Ventures. Proximity to those stakeholders is regarded as critical to the firm at its current incipient stage of development. The company also attaches value to being in Cambridge's academic environment and to the cache of having a Cambridge address. Taxes are not a significant influence on its locational decisions as its offices are only 13,000 square feet and government is generally not important to Ensemble as aside from permitting, it has no experience of working with government. Access to talent and networking issues were

[296] http://www.ensemblediscovery.com/
[297] This section is based on an interview with Edward Freedman, March 28, 2007.

also originally key considerations. In particular, there was a need for two levels of talent—the academic *and* the professional—as the other companies in Cambridge are also the employment base from which Ensemble recruits since employees change companies all the time. The biotech job market in Cambridge has become more dynamic because although it used to be that in big pharma one had a job for life, there are now layoffs as management is shedding employees to show profitability and growth to Wall Street by cutting labor costs as an expense when sales are flat. Consequently, biotech employees are moving around more and are more willing to take risks in the job market. Likewise, networking is a critical part of the decision to locate in Cambridge as from a business development perspective, when businessmen come to Cambridge, they usually visit lots of biotech companies at the same time so it is easier to network and seek out business opportunities for one's firm.

Although Ensemble valued being in Cambridge during its early phase of development it will probably move to Lexington or Waltham when its lease expires early next year as 85% of its employees reside in the metrowest Waltham area. Moreover, while the company originally acquired its lab space during a 2003 lull in the real estate market such that it is only paying $40 per square foot at present, the rental rates are rising considerably and are expected to double to $80 per square foot. Thus while the decision to start in Cambridge was driven by the need to be close to founders and funders, the decision not to remain will be financial because as they seek to take their technology to scale, cost issues are becoming a more significant consideration. In this way, the experience of Ensemble Discovery Corporation also highlights the importance of size in the locational dynamics of biotechnology firms in Cambridge. As Mr. Freedman points

out, a small firm like Ensemble is not big enough in terms of potential revenue impact or employment to have the leverage to negotiate deals with the City of Cambridge. As big companies such as Genzyme and Novartis pick up large chunks of Cambridge real estate for their operations and thereby put upward pressure on the real estate market, it is becoming harder to find those smaller plots of real estate that would previously have been broken up into many small chunks for use by startups. It has become very difficult for smaller companies in Cambridge to find a 20,000 square foot space for their operation. However, Mr. Freedman also points out that moving to Lexington and Waltham does not mean moving far as they are developing into mini-clusters that complement the mega-cluster in Cambridge. The fact that firms of the caliber of Astrozeneca are in Waltham is indicative of the growing significance of the area. But the major issue is cost. Instead of paying $60-80 per square foot, these satellite biotech clusters charge $35-40 per square foot and they do not charge for parking which is huge cost as Ensemble is currently paying $135 per month for each employee's parking spot. Thus, firm size is a key influence over its locational decisions as larger firms have a greater capacity to absorb the high cost of being part of the Cambridge milieu.

This matrix summarizes the factors influencing the locational decisions of the aforementioned firms:

Matrix of Factors Impacting Decision to Locate in Cambridge

	Firm	Genzyme	Pfizer	BMS	Idera	Ensemble
Factor						
Talent in Cambridge		X	X			X
Access to Technology						
Taxes						
Local Assistance (Permitting, etc.)						
Local Infrastructure					X	
State Incentives				X		
Access to Federally Subsidized Pre-Commercial R&D		X				
Federal Policy (i.e. ODA)		X	X			
Proximity to Hospitals		X	X			
Proximity to Founders						X
Networking		X	X		X	X
Availability of Lab Space					X	
Cost of Lab Space						X

Talent and networking are critical to almost all firms but for the larger firms the hospital network and federal policies with regards to patents, as well as the Orphan Drug Act and support for research funding at hospitals are also important. Likewise, access to the technologies of startups, and those commercialized by universities as a consequence of the Bayh-Dole Act is also significant.

Part X: An Analysis of the Role of Federal Policy in the Development of the American Biotechnology Industry

Federal policy has played a critical role in the development of the American biotechnology industry in that it has contributed to the evolution of a symbiotic relationship between small biotechnology start-ups and multi-national pharmaceutical corporations, both foreign and American. That is a key driver in the development of biotechnology clusters. How has the policy context in the United States affected the development of the biopharmaceutical industry? Amongst the specific U.S. policy changes that promoted commercialization are:[298]

Major U.S. Policy Initiatives Favoring Science-Based Entrepreneurship

Name and Date	Description	Implication for Entrepreneurship
Stevenson-Wydler Technology Act (1980)	Facilitate the transfer of technologies that originated and are owned by Federal Laboratories to the private sector.	Employees could become entrepreneurs by licensing technology developed at Federal Labs. Other firms could view Federal Labs as a source of technology for transfer.
Bayh-Dole University and Small Business Patent Act (1980)	Permitted small business, universities and not-for-profit institutions to retain title to inventions resulting from federally funded grants and contracts.	Encouraged universities to actively engage in technology transfer to license inventions to industry. Allowed federal contracts to engage in commercialization.
Small Business Innovation Development Act (1982)	Established the Small Business Innovation Research Program within major federal agencies.	Increased funding available for technologically-oriented small business.

[298] Venture Economics and Maryann Feldman "The Entrepreneurial Event Revisited: Firm Formation in a Regional Context." *Industrial and Corporate Change*, volume 10, number 4, 2001.

Orphan Drug Act (1983)	Grants tax reductions and marketing exclusivity or a 20 year monopoly to companies that develop drugs to treat "orphan diseases," which are defined as those that affect fewer than 200,000 people.	Catalyzed increased research and development in biotechnology solutions to treat diseases such as cystic fibrosis, glioma, multiple myeloma and snake venom. From 1/83 to 6/04, 249 orphan drugs have received marketing authorization versus 10 in the decade prior. *The Act was critical to the expansion of Genzyme.*
National Cooperative Research Act (1984)	Eased antitrust penalties on cooperative research.	Facilitated joint projects and made it easier for small firms to find niche markets with emerging technologies
Federal Technology Transfer Act (1986)	Amended the Stevenson-Wydler Act to authorize Cooperative Research and Development Agreements (CRADAS) between federal agencies and private firms.	Allowed small firms to extend R&D capabilities by collaborating with federal labs and agencies on commercialization.
National Competitiveness Technology Transfer Act (1989)	Part of a Department of Defense authorization bill, amended the Stevenson Wydler Act to allow government-owned contractor-operator labs to participate.	Increased the pool of potential partners and research projects.
Defense Conversion, reinvestment and Transition Assistance Act	Initiated the Technology Reinvestment Project (TRP) to provide technology development, deployment and training needs of companies adversely affected by defense conversion.	Allowed firms that previously engaged in defense related business to initiate new product lines.

The policy changes combined with an entrepreneurial climate and ready access to venture capital has proven to be catalytic in fostering the growth and development of numerous successful biotechnology firms in the US. Consequently, it demonstrates the critical role of federal policy in creating an environment that it is critical to the financing of scientific innovation, the incubation of those innovations in major research universities, and the pushing of those innovations into the private sector where they can be commercialized by startups before being marketed and further developed by global pharmaceutical firms. The role of the federal government in financing innovation is particularly important in that drug industry expenditures for research and development, while large, have consistently been far less than profits.[299] For the top ten companies, they amounted to only 11% of sales in 1990, rising slightly to 14% in 2000.[300] The biggest single item in the budget of pharmaceuticals is neither R&D nor even profits but "marketing and administration"—in 1990, a staggering 36% of sales revenues went into this category, and that proportion remained about the same for over a decade.[301] At present, it is two and a half times the expenditures for R&D.[302] Thus the small startups that spinoff from publicly funded university research are where most of the critical innovation in the biotechnology arena takes place while the larger firms market those innovations after having acquired the firms.

The expansion of biotechnology in the U.S. was facilitated by the Bayh-Dole University and Small Business Patent Act of 1980 that permitted small businesses, universities and not-for-profit institutions to retain title to inventions resulting from

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[299] Marcia Angell. The Truth About Drug Companies. 2004. (Random House: New York).
[300] Ibid.
[301] Ibid.
[302] Ibid.

federally funded grants and contracts. Likewise, the Orphan Drug Act of 1983, which granted tax benefits and exclusive marketing rights to companies that develop drugs to address diseases that affect fewer than 200,000 people, facilitated increased investment in biotechnology so as to develop innovative and novel treatments for diseases for which there was a limited market incentive to find a solution. As stated earlier, the market exclusivity and tax reductions provided by the Orphan Drug Act were critical to the growth and development of major biotechnology companies such as Genzyme. The vitality of the U.S. milieu and the attendant importance of public policy have been reinforced over the years by numerous aforementioned subsequent policy initiatives. As a consequence of this supportive policy milieu—orchestrated from the Washington, DC-Baltimore, MD area—life science technology financed by government agencies such as the National Institutes of Health has been used to form numerous biotechnology firms in the U.S.

Summary

In this section, I have explored the science of biotechnology, its commercial drivers, and its origins in European innovations. I have also demonstrated how specific federal policy choices in U.S. catalyzed the development of the biopharmaceutical industry. The federal government's impact occurs through the incentives of the health care system; federal spending on university research and development and the policies governing the disposition of that research; and the FDA's regulatory policies. Specifically, as U.S. chemical companies were confronted with the commercial and scientific challenges posed by the revolution in molecular biology, policies enacted by the U.S. government played a critical role in pushing scientific innovations out of

academia into the private sector where they could be incubated in small start-up firms and commercialized by large pharmaceutical firms that had the ability to bring them to market. It is critical to note that the U.S. originally trailed European nations in biotechnology but surpassed Europe due to the policy choices it made. In the United States, which has three distinct layers of government—federal, state, and local—when one level of government decides to discontinue investment in an area of science (i.e. stem cells), other levels are free to continue it. Thus there is greater opportunity for policy innovation in the United States.

The manner in which policies in both the United States have been able to impact the industry also demonstrates that comparative advantage in biotechnology can be created or significantly influenced through governmental action. This is particularly evident in the United States, which despite advantages of size and scale, initially trailed Europe in the science of biotechnology but has succeeded in commercializing that science because of sound policies such as the Bayh-Dole and Orphan Drug Acts. The power of policy and the imperative of decision-making involvement by a range of industry stakeholders—including academic and private sector—is increasingly evident from examinations of the dynamics of the biotechnology industry.

Although trade group advocates such as Tom Finneran, formerly the head of the Massachusetts Biotechnology Council, contend that federal policy plays little role in the locational decisions of biotechnology companies, it is evident that this is not so. That the Boston/Cambridge area and Northeast Corridor which annually attract 1/3 of federally funded research expenditures—that finance both innovation and the training of talent—in the biotechnology sphere is also a key location for American biotechnology companies

indicates that federal sector and human resource development policies are a critical magnet and therefore have a profound influence on the locational decisions of both local and global biotechnology firms.

Part XI: An Analysis of the Role of State Policy in the Development of Biotechnology in Massachusetts

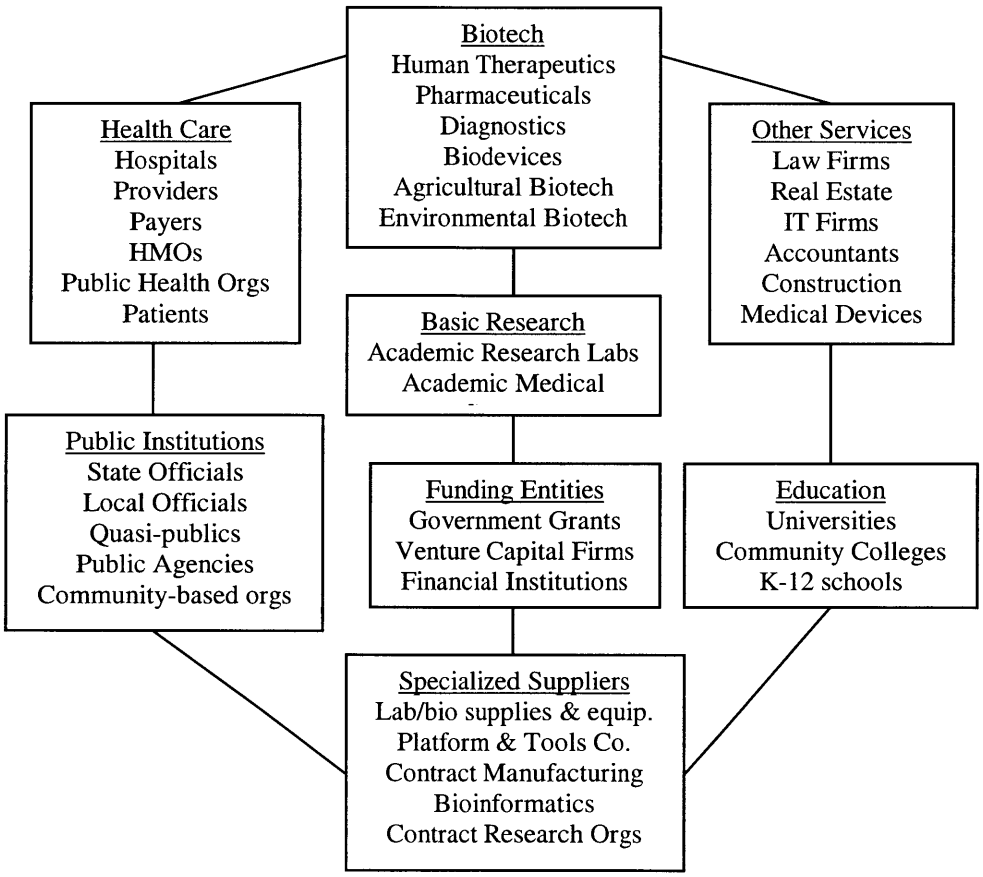
This section will explore the role of state policy in the biotechnology industry in the Cambridge/Boston area. The argument herein is that state policy has not heretofore played an especially critical role in the development of the biotechnology in the Cambridge and the locational decisions of the firms that elect to locate and remain there. However, as shall be demonstrated, in view of specific trends, state policy is critical to the future vitality of the biotechnology industry in the locations in question and Massachusetts generally.

Through fiscal policy, permitting and state supported initiatives in workforce development and general support for educational and health care institutions, the state does play a role in the cluster. Specific examples of these initiatives are delineated above in Education and Training Infrastructure and below. However, given that the two most important institutions in the cluster are Harvard University and the Massachusetts Institute of Technology—private academic organizations that have independent endowments and are able to harness hundreds of millions in federal funding—the argument herein is that the role of the state is not as important as the role of the federal and local governments.

The economic salience of the industry to Massachusetts is considerable not so much in term of employment—only about 1% of the population works in biotech—but in that as of 2002, biotechnology accounted for 18% of the state's venture capital investment, 27% of its research and development spending, 1/6 of its public companies

and approximately 10% of its market capitalization.[303] The industry attracts capital, whether it be federal research dollars, venture capital or investment from pharmaceutical companies that in turn creates additional jobs. Although biotech accounted for only 5% of all industrial jobs in the state, it accounted for ½ of the net growth—12,000 out of 24,000—of such jobs between 1996 and 2001. Moreover, the impact is even greater when the role of biotechnology as an integral part of the broader health care/life science cluster is taken into account:

Massachusetts Life Science Cluster[304]



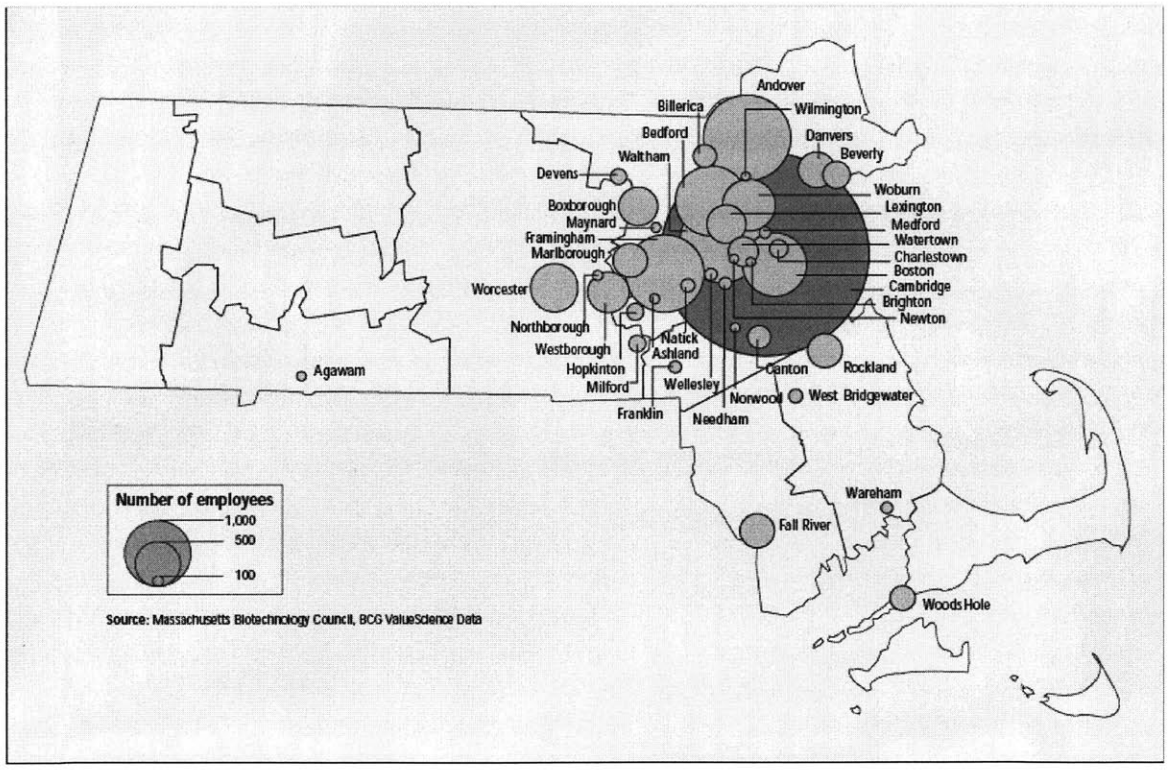
[303] Ibid.

[304] Derived from MassBiotech 2010: Achieving Global Leadership in the Life Sciences Economy. Massachusetts Biotechnology Council, 2002.

Fully 13% of the state's total employment is in the health care/life science sector which is described in this figure.[305] The above cluster diagram is more detailed than previous diagrams as it highlights each of the key actors in the state life sciences cluster and integrates the biotechnology and health care stakeholders.

As is evidenced by this map, the vast majority of those employed in the state of Massachusetts' biotech cluster are located in the Cambridge area:

Geographic Distribution of Massachusetts Biotechnology Employment, 2001[306]



The state of Massachusetts has supported the biotechnology industry in numerous ways. State support began in the early 1980s when the Massachusetts Biotechnology

[305] MassBiotech 2010: Achieving Global Leadership in the Life Sciences Economy. Massachusetts Biotechnology Council, 2002.

[306] Ibid.

Council was formed with state support following the suggestion of the governor that the industry organize itself to more effectively present a coherent set of needs to the state. The MBC has proven to be one of the most successful state biotechnology advocacy organizations as it coordinates with the Council of State biotechnology organizations, and national organizations such as BIO; runs a purchasing consortium of 10 companies to aggregate their purchasing clout so that they can obtain a 10-15% discount; and runs an annual series of about 5-7 networking opportunities and seminars and conferences on new science and new business models for its members.[307] In particular, MBC is renowned for its BioTeach program, a public-private partnership created to promote science education in Massachusetts high schools. Under BioTeach which has received both a $1.3 million grant from the federal government and $500,000 in state funding in 2006 to cover the cost of teacher and guidance counselor training, MBC works with schools to build self-sustaining programs in the life sciences, increase student literacy and career awareness in the life sciences, and address the state's shortage of skilled life sciences workers.[308] State support in terms of organization, consultation and coordination expanded in the 1990s when the government appointed a biotechnology specialist to provide the state with direct outreach to the Massachusetts Biotechnology Council.[309] Since then, state governors have regularly met with the leaders of the biotechnology community to discuss their concerns and revise the state's approach to supporting the industry.

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[307] Interview with Thomas Finneran, January 18, 2007.
[308] "Assessing the MassBiotech 2010 Report in 2006: Status Report and Follow on Recommendations for the New Gubernatorial Leadership." MBC, 2006.
[309] Breznitz, Shiri. Manufacturing Biotechnology in Massachusetts. MassBenchmark. 2006. vol 8, issue 1.

Another area of state support is in human resource development. In the area of biotechnology workforce development, in the 1980s, the state provided a 50/50 funding match to the Massachusetts Biotechnology Council for worker training.[310] Public colleges and universities such as the University of Massachusetts, and Worcester State College have established and financed biotechnology training programs to provide the industry with the personnel that it needs. Also, the state has financed the development of advanced research facilities such as those at University of Massachusetts Medical School in Worcester and the Massachusetts Biomedical Initiatives in Worcester—an organization that provides technical assistance and support for biotechnology start-up companies.

The state of Massachusetts has also played a role in assisting biotechnology firms with the infrastructure issues that are critical to their success. For example, MassDevelopment, a state agency, administers a series of loan funds to help firms with facility construction and expansion as well as the purchase of equipment. The state has also directly assisted in the land development process through the disposition of surplus state land at the former Boston and Worcester state hospitals. It has also played a role in the direct development of major infrastructure such as Interstate 290 and the refurbishment of the MBTA Red Line that linked emerging centers of biotechnology research to Boston and the region as a whole. The state government has indirectly supported the costs of development through Public Works Economic Development Program grants that cover the cost for local roads and infrastructure adjacent to biotechnology facilities. Relatedly, since the 1980s, the state has played a regulatory role in helping its municipalities such as Cambridge and Worcester to implement their zoning by-laws in a manner that is consistent with the guidelines of the National Institutes of

[310] Ibid.

Health that biotechnology firms must adhere to. Finally, the state has played a role in marketing Massachusetts as a location for biotechnology companies through its active participation in national biotechnology trade shows and conferences such as BIO.

Despite these numerous initiatives, state policy has been viewed by biotechnology industry stakeholders as insufficient to meet the needs of the industry. According to Prof. Charles Cooney[311] of MIT, state policy is not that relevant because companies locate in the Cambridge/Boston area to take advantage of the density of academic institutions and the people and technology that they provide at multiple levels in terms of management, science, faculty advisors and labs. He believes that the state government is relevant in that it is perceived as friendly to the industry and provides clear rules of the game for firms but that the talent within the cluster is of paramount importance. Cooney also believes that while Massachusetts is expensive it is more affordable than California and the density of the Boston and Cambridge makes it easier to physically meet and network with other industry stakeholders and this in turn makes it "sticky" for firms as it facilitates the personal relationships that foster the social capital so critical to innovation in the biotechnology industry. A local real estate developer[312] argues that state government has a minimal impact through tax policy but concurs with Cooney in that this individual believes that the central concern for firms that locate in Cambridge is the attraction of the talent base.

Ironically, the Massachusetts Biotechnology Council, an advocacy organization that has long had the support of the state government has been the most critical of the state's efforts to support the biotechnology industry. According to Thomas Finneran, the

[311] Interview with Charles Cooney, February 8, 2007.
[312] Interview, January 30, 2007.

former head of the MBC, from the standpoint of the biotechnology industry, the three most important elements of state policy are workforce development, permitting and tax increment financing.[313] He believes that the state needs to do more in two of these three areas. Finneran contends that tax increment financing is a powerful draw for biotechnology firms. This fiscal policy is attractive because it allows firms to work out an arrangement whereby the gains in the value of land due to improvements made are not subject to full taxation immediately but rather extend over a period of 5-7 years.[314] This is critical for biotech firms which typically lose money during their first few years of existence. Another tax policy that Finneran cites as influencing the locational decisions of biotech firms is that in Massachusetts taxes are calculated according to "single sales tax factor". This is appealing to global firms such as Novartis as their tax charge is calculated on the basis of sales within the state instead of global sales. In spite of the appeal of these fiscal policies, Finneran and the MBC, as evidenced by its position statements in the MassBiotech 2010 report, have been critical of the state's policies in other areas.

Finneran contends that the state needs to improve the permitting process. In his view, it is too litigious, needs more transparency and most importantly it is too long as it can take at least 6 months for permit approval.[315] He regards this problem as the result of home rule which has resulted in a policy context in which there is not a county setting standards but rather local control is strong and localities don't see any gain in being receptive to economic development so they resist things.[316] State support for

[313] Interview with Thomas Finneran, January 18, 2007.
[314] Ibid.
[315] Ibid.
[316] Ibid.

infrastructure is also regarded as critical, particularly in terms of water and sewage which are big issues for the manufacture of biotech, an area that the state trails in.

The aforementioned BMS deal is indicative of how the Massachusetts state government is willing to provide deal-based company-specific assistance to biotechnology firms. It is also not an isolated instance. In November 2004, Avant Immunotherapeutics opened a pilot manufacturing facility in Fall River, Massachusetts. MassDevelopment, a state agency, assisted Avant in obtaining below-market loans of up to US$2.2 million for the building and new equipment.[317]

Like Cooney, Finneran believes that the great draw for Massachusetts is the incredible concentration of teaching hospitals and educational facilities in the state so the science and technology policies of the state are not regarded as important. The one area in which that might be the case is stem cell research. Until recently, Massachusetts law in this area was rather cumbersome due to Roe v. Wade restrictions on fetal research but two years ago this language was repealed so that stem cell research is statutorily encouraged but not funded by Massachusetts. In 2006, a bill was passed that endorsed what the MBC regards as reasonable and flexible regulation and appointed a state advisory committee comprised of experts on stem cell research and related issues whose responsibility is to make recommendations to the state Department of Public Health on further laws and regulations.[318] The legislation granted the DPH statutory oversight of stem cell research but prohibits DPH from impeding or otherwise interfering with stem cell research whose parties and sponsoring institutions have met the requirements set forth in the law. Moreover, both Harvard and MIT have established private initiatives to

[317] http://www.siteselection.com/features/2005/jan/bio/

[318] "Assessing the MassBiotech 2010 Report in 2006: Status Report and Follow on Recommendations for the New Gubernatorial Leadership." MBC, 2006.

study stem cells so the federal restrictions have not affected the state in the view of Mr. Finneran. However, another criticism of state policy lodged by Finneran is that although Massachusetts is regarded as the best locale for biotech talent in the US, the industry is still concerned about the adequacy and sufficiency of the workforce. This concern is evident in a recent survey of the biotechnology industry in which respondents indicated that gaps in K-12 education were producing a local workforce that is inadequately prepared to work in the biotechnology sector.[319] Specifically, math and science training are viewed as inadequate.[320] The study recommended that the state government intervene to maintain Massachusetts' differentiation and competitive advantage in biotechnology by using public resources to strengthen the state's workforce in this area.[321] Thus government is regarded as having a critical role to play in cultivating the talent that the business community views as essential to the viability of the biotechnology industry.

The concerns of Mr. Finneran were reflected in the criticisms evidenced in the MBC's MassBiotech 2010 report. Therein it is argued that the state needs to create the right leadership team to champion Massachusetts at the federal level; develop a statewide life science research and innovation framework; streamline the regulatory framework; collaborate better with local communities; focus on biomanufacturing; and improve science education at the K-12 level.[322] Amongst the specific policies recommended are:[323]

> 1) Reinstate the position of secretary of economic affairs with a mandate and the resources to capture economic development opportunities in the life sciences.

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[319] Super Cluster. 2007. A joint publication of the Massachusetts Technology Collaborative, PriceWaterhouseCoopers and the New England Healthcare Initiative.
[320] Ibid.
[321] Ibid.
[322] MassBiotech 2010: Achieving Global Leadership in the Life Sciences Economy. Massachusetts Biotechnology Council, 2002.
[323] Ibid.

2) Appoint a science and technology senior advisor who is respected by the life-sciences cluster and aware of the challenges it faces. The senior advisor should report directly to the governor and steer the key initiatives undertaken by the new administration.
3) Introduce and support legislation (including legislation on stem-cell research and biodefense) that will enable life-sciences organizations to operate and innovate within a clear and predictable framework.
4) Work with industry, public agencies, and local communities to identify promising sites for future biotech development, streamline the permitting process, and plan the physical infrastructure.
5) Establish a science education advisory board to define the priorities, identify curriculum synergies across the state's different school systems, and initiate changes at all levels of education.
6) Make a commitment to stabilize the tax environment and make the investment tax credit permanent at 3 percent.
7) Change the legal definition of an R&D corporation and file appropriate legislation to ensure that all life-sciences start-ups can benefit from the status.
8) Encourage state pension funds and other public investment funds to invest in start-ups and early-stage venture capital funds.
9) Promote collaboration initiatives among public universities, public agencies, and the industry, in particular on homeland-security issues.
10) Communicate broadly and often about the importance of biotechnology to the state in order to create positive perceptions of biotechnology in the minds of decision makers and the public.

Since the release of the report, several of those concerns have been addressed by the state government. Amongst the actions taken to address the MBC's concerns about state policy towards the biotechnology sector are the passage of an economic stimulus package in 2003 that is known as Economic Stimulus I.[324] This stimulus package redefined an R&D corporation in such a way that is beneficial to biotechnology companies. Prior to 2003, biotech companies that did not meet a receipts test were technically not regarded as R&D corporations in the eyes of the state Department of Revenue.[325] At present, pre-profitability biotech companies that demonstrate a certain level of R&D expenditures are eligible to take advantage of sales and use tax exemptions granted by the Department of

[324] "Assessing the MassBiotech 2010 Report in 2006: Status Report and Follow on Recommendations for the New Gubernatorial Leadership." MBC, 2006.
[325] Ibid.

Revenue.[326] Economic Stimulus I also included funding to support more industry-academic collaborations and approved $25 million for the Emerging Technology Fund, which provides grants and loans to qualified companies that locate or expand in Massachusetts.[327]

To further assist the biotechnology sector, in 2006, as part of Economic Stimulus II, the state approved a further $10 million for the Emerging Technology Fund, which has proven to be so effective in attracting and retaining firms in Massachusetts that almost all of its funds have been committed. The House also approved a measure that allows municipalities at their option only - to treat biotechnology companies like manufacturing companies for tax purposes and thus exempt biotech companies from personal property tax assessments. This tax policy can be used as an incentive to attract biotech companies, which had begun to be deterred by the onerous personal property taxes levied on growing biotech companies that formerly leased equipment instead of buying it. The Legislature also authorized $50 million over 5 year for the creation of a Life Science Institute—an independent agency to coordinate the myriad activities and investments that the state government has approved or has proposed for the biotechnology industry. The LSI is modeled after similar initiatives in North Carolina and Washington state and will serve to concentrate and focus state resources in a targeted manner. It will provide incubator funds for small startups which are especially critical given that venture capital funds have become more difficult to obtain without a well-defined proof of concept and clear progress in clinical trials.[328] This is problematic as given that venture capitalists focus on biotech investments with high returns, there is not a lot of capital for good ideas that may

[326] Ibid.
[327] Ibid.
[328] Interview with Thomas Finneran, January 18, 2007.

not be as lucrative but that have substantially beneficial impacts on public health.[329] Also under consideration is the creation of a statewide biomanufacturing network under the administration of the University of Massachusetts and centered at the UMass-Lowell and UMass-Dartmouth campuses. The goal of this initiative would be to provide outsourced manufacturing capacity for emerging companies. By leveraging the infrastructure of the university and marrying it to industry expertise, this biomanufacturing initiative will seek to keep biomanufacturing jobs that support the middle class in the state. Finally, the issue of streamlining permitting has also received attention as a new law—Chapter 43 D of the Massachusetts General Laws—was passed which requires that cities and towns must vote to opt in to a system of streamlined permitting, which can include creating an office to coordinate the functions and schedules of the various boards having land use permitting and regulatory oversight.[330] Nonetheless, the fact that the new law does not give cities and towns an incentive to opt in to the streamlined and expedited permitting process is regarded as an important defect.

The argument herein is that while state policy has been trumped by talent as a key driver of the locational decisions of firms in the Cambridge/Boston area, it is increasingly important to the development of the industry. This is because as other localities in the United States and abroad have explicitly used state directed policies to become more competitive with Massachusetts, coordinated state leadership has become an increasingly important factor in recruiting firms—as evidenced by the Fort Devens case and other cases such as Singapore. Also, in order to attract the biomanufacturing jobs that support the middle class, it is important to play a role in assisting with infrastructure development

[329] Interview with Jonathan King, March 23, 2007.
[330] Interview with Thomas Finneran, January 18, 2007.

for water and such as the Fort Devens case also shows. Biomanufacturing which is more space and infrastructure intensive requires a more regional approach which is best coordinated at the state level as states' seek to support startup and research and development hubs such as Cambridge with biomanufacturing hubs in orbit around those localities. For certain types of biomanufacturing—pilot manufacturing, large-molecule manufacturing, processes involving complex R&D-intensive manufacturing techniques and packaging and finishing—there is such a tremendous advantage to locating close to research and development centers and headquarters that firms are willing to pay a 20% premium to remain in Massachusetts.[331] The proposal to create a biomanufacturing network administered through the UMass system is indicative of the acknowledged importance of this.

Biotechnology Policies in Other States

State policy will be increasingly important for the Massachusetts biotechnology industry because other state governments have taken an increasingly active role in supporting the industry. Beginning in 1985 with the Interagency Task Force on Biotechnology and continuing more recently with the establishment of biotech-supporting Institutes of Innovation such as the California Institute for Bioengineering, Biotechnology and Quantitative Biomedical Research, the California state government has consistently endeavored to strengthen the relationship between industry companies and state-funded academic institutions. In 1994, California Governor Pete Wilson established the Council on Biotechnology to provide advice on policies to encourage the

[331] MassBiotech 2010: Achieving Global Leadership in the Life Sciences Economy. Massachusetts Biotechnology Council, 2002.

growth of biotech in the state. California has also been at the forefront of allocating state funds to finance stem cell research. Moreover, the UC systemwide biotechnology research and education program provides training grants to support biotechnology research and promote academic research.

Likewise, North Carolina has emerged as a biotech hub in large part due to state support for the industry. In 1981, the state established and financed the North Carolina Biotechnology Center to develop a coordinated strategy to stimulate the growth of biotechnology in the state. The NCBC is noted for its success in teaming with educational institutions to offer training programs through community colleges, teacher-training programs for K-12 and university-level programs and educational grants for work force development. The state's cumulative investment in biotechnology initiatives in 2002 was $135 million which triggered more than $2 billion in direct out-of-state investment through venture capital financing, manufacturing investment and federal research grants.[332] The following table demonstrates how Massachusetts compares to California and North Carolina as far as state policy is concerned:

Massachusetts Policy Compared to California and North Carolina: 2002[333]

	Massachusetts	California	North Carolina
Tax Policy	-10% R&D tax credit -3% credit in depreciable assets -Single sales factor	-15% (in-house) and 24% (outsourced) R&D tax credits -100% net operating loss carry forward -7% job-creation -6% manufacturing credit	-5% R&D tax credit -7% tax credit for machine and equipment leases
State Support for Innovation	-Massachusetts Biomedical Initiatives	-State collaboration with industry and state universities to develop	-State-funded North Carolina Center for Biotechnology

[332] Ibid.
[333] Derived form MassBiotech 2010: Achieving Global Leadership in the Life Sciences Economy. Massachusetts Biotechnology Council, 2002.

		jointly funded research programs	
State-funded Seed Capital	-$8 million cumulative MBI investment -Some state pension fund investment	-$500 million CalPERS Biotechnology Program	-$10 million North Carolina Bioscience Investment Fund ($40 million cumulative investment over time) -$42 million-$150 million in tobacco-settlement money for biomanufacturing

Given the increased competition within the policy milieu, Massachusetts can no longer rely on its superior talent base alone as a comparative advantage.

The growing importance of state policy is perhaps most saliently evidenced by the rapid emergence of Singapore, a Southeast Asian city state that is now a major biotech hub despite the absence of any considerable capabilities in the sector as recently as a decade ago. This has been made dramatically apparent by the fact that the United States, which is usually a talent magnet, has been actually experiencing a brain drain in this promising field due to funding restrictions. Specifically, two of America's most prominent cancer researchers, Dr. Neal Copeland and Dr. Nancy Jenkins, are amongst several leading U.S. scientists who out of disillusionment with politics and budget cuts in stem cell research have been recruited by the Singaporean government to take posts at its Institute of Molecular and Cell Biology.[334] Singapore has successfully become a force in the biomedical industry through an integrated strategy that entails the development of world class infrastructure—Biopolis is a $250 million, 2 million square foot facility that will serve as the home for five biomedical research institutes (the Bioinformatics Institute, the BioProcessing Technology Institute, the Genome Institute, the Institute of Molecular and Cell Biology and the Institute of Bioengineering and Nanotechnology).

[334] "Science Haven in Singapore." New York Times, August 17, 2006.

The country has successfully attracted tens of millions of dollars in investment from world class biopharmaceutical firms such as GlaxoSmithKline and Novartis, which has located its Institute for Tropical Diseases in BioPolis. Moreover, they have made an explicit commitment to attracting foreign talent to jump start their biotechnology industry, just as the Singaporeans have done in the past when the government transformed Singapore into a home base for multinational companies doing business in Southeast Asia. The recruitment of foreign talent—especially scientists disaffected by research restrictions that may prevail in other countries—and large firms is an explicit part of the Singaporean strategy for development of the biotechnology industry. The Singaporean government has also made grants for research and development projects, investment allowance for new equipment, and technology training available along with reduced corporate taxes and full tax exemptions so as to recruit firms to what it deems to be a strategically vital industry. Finally, investment by Bio*One Capital, a government-linked life sciences fund with a $1.2 billion portfolio is being used as a mechanism to acquire technology that can be brought back to Singapore while the Singapore Economic Development Board supports startups by matching third-party investments in early-stage companies dollar for dollar, up to $300,000.[335] The net result of these physical infrastructure, human capital and firm recruitment, and investment strategies is that biotechnology is booming in Singapore.

[335] "Top Five Regions Targeting Biotech Companies." FierceBiotech, January 25, 2006.

Summary

In the case of Cambridge, Massachusetts state fiscal policies—tax increment financing and single sales factor—have not played a critical role in the attraction and retention of biotechnology firms. But it is the incredible agglomeration of human and scientific capital that is often supported with some state financing that is the major attraction of the state. However, as the state endeavors to attract biomanufacturing plants in an increasingly competitive milieu, state policy will be increasingly important to the viability of the industry. This is evident in the below table which highlights both the role that myriad Massachusetts policy tools are playing in the biotech industry and the view of those tools that the business community has:

Major Massachusetts Policy Tools for Biotech Industry

Policy Tool	Implication for Biotech Industry (based on interviews)
Infrastructure	High. To attract biomanufacturing in a competitive context, state must increasingly subsidize infrastructure improvements.
Zoning & Permitting	High. As space become scarce and given desire to attract biomanufacturing, state must facilitate zoning and expedite permitting. Biotech buildings have specific requirements so this is always a strong concern of business.
Marketing	Moderate. MA is already well known as an R&D site. Key factor in getting attention of corporate decisionmakers vis a vis biomanufacturing.
Tax Policies: Tax Increment Financing & Single Sales Factor	Low. Firms locate in MA in spite of costs.
Hospitals	Moderate. Access to publicly funded hospitals is an essential part of the industry value chain but most of this funding is from federal sources such as NIH.
State Supported Education & Training	Moderate. Most important public funding of education and training comes from federal research grant. However, there are long term concerns that K-12 education is failing and access to talent is a key driver for the biotech industry.

To compete both nationally and internationally, the state must play a lead role in coordinating regional efforts, developing supportive infrastructure, addressing permitting concerns and marketing the state to compete with other locales. This is already evident in the state's efforts to recruit Bristol-Myers Squibb and Avant Therapeutics. A regional approach is also critical because as the biotechnology industry evolves in the area, Cambridge, which is a part of the Northeast Corridor regional innovation system, is becoming the hub of its own regional innovation that includes the surrounding communities of Waltham, Lexington, and Framingham.

Part XII: An Analysis of the Role of Local Government in the in the Locational Decisions of Cambridge Biotechnology Firms

The central argument herein is that relative to state and federal government, local government policy has been the most significant aspect of governmental impact vis a vis the locational decisions of biotechnology firms in Cambridge. However, its impact has been inadvertent as well as intentional. Specifically, strict guidelines to govern the operation of biotech firms, and designed to limit biotech development in Cambridge, created just the framework of stable, consistent standards—however high—that the industry needed for growth. Since biotechnology firms incubate technology for long periods of time, clarity and consistency of policy are critical influencing factors in the decision to invest in a specific locale for an extended time horizon. The considerable talent endowment of the Cambridge area is, of course, a significant factor but that talent operates in a locational context that is influenced by local government more so than by any other level of government.

Local government policy in Cambridge has played a key role in the locational decisions of biotechnology firms. The key element is that in the late 1970s and early 1980s, Cambridge was one of the first cities in America to establish a clear set of rules and regulations, albeit tough ones, with regard to the emerging technology of recombinant DNA.[336] As a consequence business knew what to expect from the

[336] Interview with Charles Cooney, February 8, 2007.

beginnings of the industry.[337] According to a key actor in both the City's policymaking and real estate milieux, the key event was in 1974 when by accident Cambridge established a positive regulatory environment for biotechnology.[338] In 1974, Harvard University had converted an older biology building to do recombinant research which was very controversial at the time. Cambridge suspended this activity until it could be studied and the City debated if it should allow privately financed research to be done unfettered. Then NIH put forth safety standards and there was a voluntary moratorium due to the safety standards. What emerged was a series of regulations and protocols for organizations that got federal funds. In 1976, the City of Cambridge's Biohazards Review Board, then imposed the same standard on private and federal research and prohibited PH labs (germ warfare labs). It did not matter if one received federal or private funds. The objective was to stop the research but ironically the common standard acted as a spur for biotech growth as Cambridge was the first area that had both talent and a set of understandable standards and rules so research could occur in Cambridge. Businessmen were afraid to go to other uncertain communities where you could sign a 15 year lease and then have the rules changed on you. As a consequence, in trying to make it more difficult for the biotech community, local government initiated a strong and stable marriage between the local talent base and a clear and reliable, albeit stringent, regulatory regime that due to the long term commitments required by the industry was actually more favorable to firms.

In addition to its regulatory role, local government emphasizes that it endeavors to help with permitting and the processing of the paperwork necessary to meet the City's

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[337] Ibid.

[338] The remainder of this section is based upon an anonymous interview, January 30, 2007.

requirements, particularly with regards to health issues.[339] Its contention that it does a good job with permitting is called into question by Tom Finneran, formerly of the MBC, as well as by Mr. Hillback's contention that in the business community, Cambridge is referred to as the "independent socialist republic of Cambridge."[340] A local real estate developer argues that better zoning would help as biotechnology firms do not want to move since they grow in phases.[341] They do not want to locate in a particular place in phase 1 and then have to expand elsewhere in phase 2 but there is a bias in Cambridge to try to reduce density which makes it difficult for firms.[342] Firms are willing to tolerate this in part because real estate is only 10% of the burn rate for biotech firms and 70% is spent on talent.[343] The experience of Genzyme, which is illustrated below, as it has attempted to grow while remaining a part of the Cambridge milieu is an example of the lengths to which firms will go to stay in the Cambridge area.

While the City of Cambridge does not provide any fiscal assistance as it does not grant monetary incentives to firms, and this also includes no provision for infrastructure, it does endeavor to foster collaboration and information provision. [344] According to Ms. Johnson, the City of Cambridge is involved in the back end of locational decisions—after firms make the decision or while they are deciding.[345] As she sees it, these are internal corporate decisions.[346] This is done through informal meetings, marketing the City, and information dissemination. However, as is the case with its permitting efforts, the private sector has been somewhat critical of city government. According to Mr. Hillback, as a

[339] Interview with Estella Johnson, January 29, 2007.
[340] Interview with Elliott Hillback, March 9, 2007.
[341] Interview, January 30, 2007.
[342] Ibid.
[343] Ibid.
[344] Interview with Estella Johnson, January 29, 2007.
[345] Ibid.
[346] Ibid.

big firm, Genzyme does not look to government for collaboration and information and he doubts that any firm would really look to government to make connections for them.[347] In his view, venture capitalists, the MBC, and hospitals are better for making connections.[348] Although, the efficacy of its efforts to foster collaboration may be called into question, Cambridge does not do much in terms of fiscal policy because, until the recent emergence of competition from other locales, it has not had to. Even in the Fort Devens case, it was the state, which was run by a governor who had made significant wealth in the biotechnology industry as a venture capitalist with Bain Capital, that intervened to induce the establishment of a much needed biomanufacturing plant. Because of the attraction provided by its intellectual, social and technology capital along with a strong and reliable regulatory regime, the Cambridge local government does not have to provide direct monetary inducements to the biotechnology industry.

Space is also a critical factor in the locational decisions of biotechnology firms in Cambridge. In the late 1970s and early 1980s, the area in Cambridge around MIT had lots of empty warehouse, which made it easy for many companies, particularly local university spinoffs to find space and remain in the area as firms were able to rent or purchase existing buildings close to their research university and potential labor force.[349] The large amounts of warehouse space in Kendall Square—before its current reinvention as a technopole—provided the necessary real estate for entrepreneurs to establish biotechnology startups with all the lab facilities and physical specs required. According to a local real estate developer, the character of these spaces—high ceilings, strong floors—has influenced the locational dynamics of the biotechnology industry in

[347] Interview with Elliott Hillback, March 9, 2007.
[348] Ibid.
[349] Breznitz, Shiri. Manufacturing Biotechnology in Massachusetts. MassBenchmark. 2006. vol 8, issue 1.

Cambridge. Cambridge has evolved into a center for biotech research and development—as opposed to biomanufacturing—because the high ceilings and strong floors turned out to be perfect for a wide variety of lab spaces which is what research oriented biotech firms require.[350] That flexibility is also in tune with the desire of developers not to build the large, open, special purpose spaces that manufacturing-oriented biotechnology firms demand.[351] Cambridge has few large open spaces to begin with.[352] Moreover, developers are reluctant to develop specialized spaces for biomanufacturing as they acknowledge that since most biotech firms lose money, they must assume that every tenant will fail so a space must be flexible enough to be handed over to another client.[353] In addition, in an area with costly rents such as Cambridge, the high cost of renting large spaces is a deterrent.

Another reason that Cambridge has not evolved into a center for biomanufacturing is that it is simply cheaper to do the manufacturing abroad where there are fewer environmental regulations and emerging areas like Puerto Rico and Singapore are willing to offer tax incentives to induce firms to locate there. Although some large firms like Genzyme keep pilot manufacturing in the area so as to be near hospitals during the testing phase, once the product is approved full scale manufacturing is often done abroad as part of a global biotechnology production system.

As the below table indicates, regulatory certainty and regulation over space are the critical policy tools that local government has brought to bear on the biotechnology industry.

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[350] Interview, January 30, 2007.
[351] Ibid.
[352] Interview with Estella Johnson, January 29, 2007.
[353] Interview, January 30, 2007.

Major Cambridge Policy Tools for Biotech Industry

Description	Implication for Biotech Industry (based on interviews)
Regulatory Certainty	High. Biotech has long time to market so high but certain standards facilitate long term investments.
Infrastructure	Low. Cambridge generally does not finance infrastructure improvements.
Zoning & Permitting	High. Space is scarce and expensive in Cambridge so this is a critical issue to firms that wish to locate in the Cambridge so as to be close to talent.
Networking	Low. Business community prefers to use industry groups to network.
Tax	Low. Cambridge does not grant tax breaks.

Talent and the physical characteristics of the spaces near that talent along with the early establishment of regulatory certainty are most critical to the biotech business community in its dealings with local government in Cambridge.

Biotechnology Policies in Other Localities

Increasingly other localities in the Cambridge area have been able to benefit from the high costs intrinsic to the Cambridge real estate market as well as the relative passivity of the Cambridge local government in working to provide firms with infrastructure and fiscal assistance. In towns like Beverly, where the cost of real estate is approximately $20-30 per square vs. $60-80 in Cambridge, the relatively cheaper price of real estate in the suburbs has become increasingly critical for small firms that plan to expand rapidly.[354] It simply makes better commercial sense from a long term planning perspective to be in a locality where one's ability to expand spatially is not inhibited by the cost of real estate. Since localities like Waltham and Beverly are only 20 and 30

[354] Demarco, Peter. "Some biotech firms bypass Cambridge for the suburbs." September 25, 2002. http://www.cummings.com/articles/biotech_globe_0926.htm

minutes respectively from Cambridge, locating in a cheaper area and commuting to Cambridge for meetings with key players in the biotech industry is easy to do. Moreover, as Mr. Freedman of Ensemble noted, the demographic profile of workers interacts with the issue of commuting time. Firms that have older employees who have started families in the suburbs are more disposed to locating outside of Cambridge to be closer to their employees' personal lives and to save on parking costs. As a consequence, since the recession of 2001-2002, biotech firms have been leaving Cambridge for the suburbs to take advantage of cheap real estate. Amongst the notable departures are: Praecis Pharmaceuticals Inc. which moved into a 175,000 square feet in Waltham; Cubist Pharmaceuticals Inc. which moved into a 88,300 square feet in Lexington; GPC Biotech AG which moved into a 85,400 square feet in Waltham; and Bio-Rad Laboratories Inc. which moved into 50,000 square feet in Randolph.[355]

Related to the issue of cost is the general scarcity of space in Cambridge. As stated earlier, biotech firms that are looking to expand face difficulties not only with regard to the cost of space but its general unavailability in Cambridge. As a consequence, those firms that wish to buy space for one big facility and keep all of their operations under one roof instead of operating from several different parcels of land that they have acquired in Cambridge as those space became available, are increasingly doing so in the suburbs. For example, Cubist, is an MIT spinoff, that began in 1992 with a single lab on Emily Street. By 2001, the company had taken over two more buildings and was looking

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[355] Bill Archambeault, Bill. "Cambridge's heady biotech growth may soon be over." Boston Business Journal - February 15, 2002.

to grow again - but chose not to do so in Cambridge because it was able to purchase a former W.R. Grace facility in Lexington, that dramatically increased its square footage from 55,000 to 88,000.[356] According to Jennifer LaVin, the company's senior director of corporate communications: "We were a little disjointed in Cambridge because of the physical space. We needed to be under one roof. And all available land in Cambridge is gone."[357] The value that firms place on the ability to expand is perhaps most saliently expressed in the example of AstraZeneca. AstraZeneca first established a research presence in Boston in 1995. In 2000, the company opened its state-of-the-art research facility in Waltham, where it has continued to invest and expand, growing from 170,000 square feet to the current 250,000-square-foot facility. On May 7, 2007 AstraZeneca announced that it has officially begun construction of a $100 million research and development facility that will increase the total size of its space in Waltham by 132,000 square feet from 250,000 square feet to 382,000 square feet by mid-2009.[358] Moreover, as firms have located in Waltham, it has emerged as a center for venture capital in the region. Polaris Ventures, a leading VC with strong ties to MIT, is based in Waltham as are Advanced Technology Ventures, Castle Ventures, Marconi Ventures, Longworth Venture Partners, and North Bridge Venture Partners. Thus as biotech firms locate to other satellite areas, the supporting ecosystem of venture capitalists and lawyers that is necessary to sustain them follows the firms.

Other localities are also benefiting from the high real estate costs and scarcity of space in the Cambridge biotech market. Cities such as Devens have been very

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[356] Ibid.
[357] Ibid.
[358] "AstraZeneca to Begin Construction for $100M Research Investment at R&D Boston." PharmaLive.com, May 7, 2007.

aggressive—unlike Cambridge—in addressing the concerns of business with regards to permitting and zoning. While the aforementioned deal to bring Bristol-Myers Squibb to Devens was facilitated through state intervention, it was also assisted by Devens itself. Devens is the only Massachusetts municipality that has a one-stop permitting process that takes less than 75 days.[359] As a consequence, BMS was able to receive its construction permits in a record 49 days.[360] Just as states have become more aggressive so as to induce firms to locate away from Massachusetts so too other localities within Massachusetts are becoming more aggressive and responsive to business concerns so as to enhance their competitiveness in the market for biotech facilities.

Conclusion

Local government has played a critical role in the locational decisions of biotechnology firms in Cambridge through the early establishment of a clear set of rules and regulations for an industry that has a long investment horizon. Those rules which were not intentionally designed to induce biotech firms to locate in Cambridge had the unintentional consequence of catalyzing the areas considerable talent base. That talent base is comprised not only of universities but of hospitals which serve as important nodes for testing and NIH sponsored research. Until recently, Cambridge has not had to offer monetary incentives to get firms to locate here but as other locales increase their competitiveness that may change. This perspective is reinforced by Mr. Johnson's

[359] Super Cluster. 2007. A joint publication of the Massachusetts Technology Collaborative, PriceWaterhouseCoopers and the New England Healthcare Initiative.

[360] Ibid.

contention that Cambridge must do more to compete for biotechnology firms.[361] Still large firms have greater latitude with regards to their locational decisions and for them cost and tax incentives are much less important than the strategic imperative of access to the talent that drives the innovation at the heart of their business. Moreover, while local government endeavors to play a coordinating and information dissemination role, it is apparent that the business community views other actors such as venture capitalists, hospitals and industry associations as better suited to that role. The influence of government is mostly saliently manifested in its role at the very beginnings of the biotech industry in Cambridge in establishing the requisite policy environment for the industry to flourish over time.

[361] Interview with Estella Johnson, January 29, 2007.

Part XIII: Dissertation Conclusion

Is Chomsky right? Does the government play a meaningful role in the locational decisions of biotechnology firms? The answer demonstrated by the evidence presented herein is that the success of the Cambridge biotechnology cluster is indeed the outcome of a distinct set of local, state and federal government policy choices. To be sure, the answer to this question is somewhat nuanced. Other factors such as the high quality hospitals in Boston that are a mechanism for testing products and that are concentrated in such a way as to encourage the social networking that is essential to innovation are also important reasons that biotechnology firms elect to locate in Cambridge. Likewise, Cambridge and its research universities are talent magnets for an industry that utilizes human capital as the primary resource. This talent in turn makes Cambridge attractive to the biotechnology industry. Likewise, through an accident of history, Cambridge has been blessed with a physical endowment in terms of the warehouse style buildings—high ceilings and reinforced floors—that are a sine qua none for the laboratory space that biotechnology firms require. If such space did not already exist in Cambridge then retrofitting buildings to accommodate the needs of the biotechnology industry might be too costly or prohibited by zoning regulations and safety considerations. Thus there are several non-government factors that have influenced the locational decisions of the biotechnology firms in Cambridge.

Still, the critical influence of government in attracting biotechnology firms is evident throughout the Cambridge milieux. Talent matters but it does not operate in isolation. Cambridge has successfully attracted scientific and medical talent to its research universities and adjacent hospitals in significant part because so much of the

research that is conducted therein is financed by the federal government through multi-billion dollar grants from the National Institutes of Health and the National Science Foundation. Access to the fruits of that federally financed labor, which the federal government has encouraged be made accessible to the private sector through the Bayh-Dole Act, is one of the major reasons that biotechnology firms place such a premium on being in close proximity to the Cambridge scientific milieu. Moreover, the tax breaks provided under federal policies such as the Orphan Drug Act can be a powerful incentive that influences the target markets that firms such as Genzyme pursue and hence also creates an added incentive of being key players in a scientific milieu such as Cambridge, where federally financed cutting edge research on obscure diseases in being pursued. Just as federal policy influences the market entry and locational policies of firms, so too federal intellectual property protection policies play a key role in the exit strategies and attendant locational decisions of firms. Once a drug is scheduled to go off-patent where it will face competition from generic drugs, firms such as Pfizer must make decisions about where to contract and expand their operations. Federal policy has a dynamic impact upon the locational decisions of biotechnology firms.

The impact of state policy on the locational decisions of biotechnology firms is only now becoming salient. Until the advent of increased competition from other areas such as North Carolina and Singapore, the state government has not been a key actor in attracting firms to the area as the aforementioned factors were sufficient in and of themselves. However, in order to sustain the biotechnology and extend its benefits by attracting the biomanufacturing plants that employ more middle class workers, the state has increasingly become a key player in marketing the state and providing tax breaks and

other incentives to biotechnology firms so as to induce them to locate in the state. This is evident in the deal that brought a Bristol-Myers Squibb biomanufacturing plant to Fort Devens. Moreover, as the biotechnology industry has regionalized with Cambridge becoming a hub surrounded by the spokes of Waltham, Framingham and Lexington, a regional approach to the industry that is best facilitated through the state government has become increasingly important. State government will be an even more important player in the biotechnology industry in the future than it has been in the past.

The role of local government in the locational decisions of biotechnology firms in Cambridge is rather interesting. From the industry's very beginnings, the City of Cambridge has actually sought to deter the biotechnology industry with strict standards. Ironically, the serendipity of a strict but stable regulatory regime gave the biotechnology industry the policy certainty that it was seeking. This along with talent and the aforementioned characteristics of the real estate environment catalyzed the development of the industry. Given that Cambridge was the first to lay out a stable, transparent set of rules, the impact of such should not be underestimated.

Government matters. This is evident not only in Cambridge, Massachusetts but also abroad in countries like Singapore that have successfully developed biotechnology clusters with governmental leadership. The U.S. trailed Europe in the science of biotechnology until governmental leadership created an environment wherein biotechnology could thrive. The evolution of the biotechnology industry in Cambridge demonstrates that entrepreneurship—the ability to organize, manage, and assume the risks of an enterprise—is a phenomenon that is not unique to the private sector. Rather it is a quality that cuts across the governmental, academic and private sectors. In the context

of the Knowledge Economy, the success of biotechnology industry in Cambridge demonstrates that entrepreneurship is essential from all three pillars of society.

Appendix

CONSENT TO PARTICIPATE IN INTERVIEW

Study Title: An Analysis of the Role of Government in the Locational Decisions of Cambridge Biotechnology Firms

You have been asked to participate in a research study conducted by Michael Sable from the Department of Urban Studies and Planning at the Massachusetts Institute of Technology (M.I.T.). The purpose of the study is to evaluate the role of government policies, public infrastructure and fiscal expenditures in the locational decisions of Cambridge biotechnology firms. The results of this study will be included in Michael Sable's doctoral dissertation. You were selected as a possible participant in this study because of your status as a stakeholder in the Cambridge biotechnology community. You should read the information below, and ask questions about anything you do not understand, before deciding whether or not to participate.

• This interview is voluntary. You have the right not to answer any question, and to stop the interview at any time. We expect that the interview will take about one hour.

• You will not be compensated for this interview.

• Unless you give us permission to use your name, title, and / or quote you in any publications that may result from this research, the information you tell us will be confidential.

• We would like to record this interview on audio cassette so that we can use it for reference while proceeding with this study. We will not record this interview without your permission. If you do grant permission for this conversation to be recorded on cassette, you have the right to revoke recording permission and/or end the interview at any time.

This project will be completed by May 2007. All interview recordings will be stored in a secure work space until (*1 year*) after that date. The tapes will then be destroyed.

I understand the procedures described above. My questions have been answered to my satisfaction, and I agree to participate in this study. I have been given a copy of this form.

(*Please check all that apply*)

[] I give permission for this interview to be recorded on audio cassette.

[] I give permission for the following information to be included in publications resulting from this study:

[] my name [] my title [] direct quotes from this interview

Name of Subject

Signature of Subject _____ Date _____

Signature of Investigator _____Date _____

Please contact *Michael Sable; 617-452-4390* with any questions or concerns
If you feel you have been treated unfairly, or you have questions regarding your rights as a research subject, you may contact the Chairman of the Committee on the Use of Humans as Experimental Subjects, M.I.T., Room E25-143b, 77 Massachusetts Ave, Cambridge, MA 02139, phone 1-617-253-6787.

DISSERTATION QUESTIONNAIRE

Interview Questions for Firms and Research Organizations

1) Tell me about your company.

2) Who are your competitors?

3) Describe the value chain for your firm?

4) How long have you been here?

5) Have you been involved in the firm's locational decisions?

6) Tell me about the decision your firm made to locate here.

7) Why did your firm choose to locate in Cambridge versus other locales?

8) Was it a controversial decision?

9) What did you think your firm considered in its locational decisions?

10) How would you characterize the role of government—local, state, and federal--in the your firm specifically and in the biotechnology industry generally? Specifically, what has been the distinct roles of federal, state and local governments?

11) Does your firm work with government directly in any way?

12) What do you wish government would do with regards to the biotechnology industry?

13) What are the challenges/constrains in finding suitable space; and building suitable space? How does your firm overcome those constraints?

14) Is there anything that I have not mentioned that you believe is pertinent to my concern with the locational decisions of biopharmaceutical firms? If so, please specify.

Additional Interview Questions:

What are the most important factors in determining where your biopharmaceutical company is located?

Supportive Government Policies? If so, which ones?

Tax Incentives?

Infrastructure? If so, what type and characteristics?

Infrastructure capacity (power, water, sewerage, waste disposal):

Ranking: [ ] Not at all [ ] A little [ ] Somewhat [ ] Pretty Much [ ] Very Much

Good transportation links:

Ranking: [ ] Not at all [ ] A little [ ] Somewhat [ ] Pretty Much [ ] Very Much

Good communications infrastructure:

Ranking: [ ] Not at all [ ] A little [ ] Somewhat [ ] Pretty Much [ ] Very Much

Availability of suitable facilities (i.e. built to company's needs):

Ranking: [ ] Not at all [ ] A little [ ] Somewhat [ ] Pretty Much [ ] Very Much

What is your relationship to research institutes? Which ones?

Proximity to research institutions to obtain intellectual property, use facilities (i.e. labs, libraries); train employees; or recruit quality workforce:

Ranking: [ ] Not at all [ ] A little [ ] Somewhat [ ] Pretty Much [ ] Very Much

Availability of specialized finance (i.e. venture capital); specialized business support services (legal); or area targeted government assistance/local economic incentives:

Ranking: [ ] Not at all [ ] A little [ ] Somewhat [ ] Pretty Much [ ] Very Much

Where do you get workers?

Quality and availability of the local workforce:

Ranking: [ ] Not at all [ ] A little [ ] Somewhat [ ] Pretty Much [ ] Very Much

Quantity of Employees:

Ranking: [ ] 1-5 [ ] 6-10 [ ] 11-25 [ ] 26-50 [ ] More than 51

Employee Skill Level:

Ranking: [ ] No Diploma Required [ ] High School Diploma [ ] College
[ ] Graduate Degree

Residential Location of Most Employees:

Proximity to customers and clients for products/services or proximity to key suppliers and sub-contractors:

Ranking: [ ] Not at all [ ] A little [ ] Somewhat [ ] Pretty Much [ ] Very Much

Proximity of colleagues working in the area/presence of local contacts and networks:

Ranking: [ ] Not at all [ ] A little [ ] Somewhat [ ] Pretty Much [ ] Very Much

Presence of similar companies for collaborations and technology spillovers:
Ranking: [ ] Not at all [ ] A little [ ] Somewhat [ ] Pretty Much [ ] Very Much

Image/"right address":
Ranking: [ ] Not at all [ ] A little [ ] Somewhat [ ] Pretty Much [ ] Very Much

Institutions for Collaboration (Chambers of Commerce; industry associations; alumni networks):

Ranking: [ ] Not at all [ ] A little [ ] Somewhat [ ] Pretty Much [ ] Very Much

Interview Questions for Government Personnel

1) Tell me about your organization.

2) How long have you been in this organization?

3) How important is the biotechnology industry to Cambridge?

4) Are there policies to encourage biotechnology? What are they?

5) Describe what, if any activities, that your organization does to support biotechnology?

6) Have you been involved in the organization's activities in this arena?

7) How much money does this organization spend to support biotechnology?

8) What policies/regulations does your organization engage in to support biotechnology?

9) Has your organization built any infrastructure to support the biotechnology industry?

10) What about tax incentives?

11) How would you characterize the role of government—local, state, and federal--in the biotechnology industry? Specifically, what has been the distinct roles of federal, state and local governments?

12) What do you wish government would do with regards to the biotechnology industry?

13) What are the challenges and constraints encountered in getting biotech space built? What do you do to overcome these challenges and constraints?

14) Is there anything that I have not mentioned that you believe is pertinent to my concern with the locational decisions of biopharmaceutical firms? If so, please specify.

Interview Questions for Non-Profits (Academic)

1) Tell me about your organization.

2) How long have you been in this organization?

3) How important is the biotechnology industry to your organization?

4) Describe what, if any activities, that your organization does to support biotechnology?

5) Have you been involved in the organization's activities in this arena?

6) How much money does this organization spend to support biotechnology?

7) What policies/regulations does your organization engage in to support biotechnology?

8) How would you characterize the role of government—local, state, and federal--in the biotechnology industry? Specifically, what has been the distinct roles of federal, state and local governments?

9) What do you wish government would do with regards to the biotechnology industry?

10) What challenges and constraints are encountered in getting biotech space built?

11) Is there anything that I have not mentioned that you believe is pertinent to my concern with the locational decisions of biopharmaceutical firms? If so, please specify.

BIOTECHNOLOGY FIRMS IN CAMBRIDGE[362]

Absolute Science, Inc.

PO Box 382366
Cambridge, MA 02238
(617) 491-2261
Fax: (617) 492-3565
Website: www.absolutescience.com
Employees: 2 in MA
History: Founded in 1999
Facilities: Headquarters, Laboratories in Cambridge, MA
Ownership: Private
Commercial Market Sectors:
Contract Manufacturing
Contract Research
Areas of Research: Synthetic chemistry, Medicinal Chemistry, Combinatorial Chemistry, Assay Development

Acambis, Inc.

38 Sidney Street
Cambridge, MA 02139-4169
(617) 761-4200
Fax: (617) 494-1741
Website:www.acambis.com
Employees: 130 in MA (180 worldwide)
History: Founded in 1990
Facilities: Manufacturing in Boston, MA; Laboratories in Cambridge, MA
Ownership: Public: NASDAQ-ACAM
Commercial Market Sectors:
Other: Vaccines
Areas of Research: Infectious Diseases **Products:**
Arilvax: Vaccine against yellow fever

Acceleron Pharma, Inc.

24 Emily Street
Cambridge, MA 02139
617-576-220
Employees: 2 in MA
History: Founded in 2003
Ownership: Private
Commercial Market Sectors: Human Therapeutics

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[362] MassBio Database.

ActivBiotics

198 Broadway
Cambridge, MA 02139
(617) 575-3000
Fax: (617) 497-9689
Website: www.activbiotics.com
Employees: 15 in MA
History: Founded in 1996
Ownership: Private
Commercial Market Sectors:
Human Therapeutics
Areas of Research: Anti-infective therapeutics, Bacterial "stealth" infections, Coronary Artery Disease, Rheumatoid Arthritis, Inflammatory Bowel Disease, and Multiple Sclerosis.

Advanced Magnetics, Inc.

61 Mooney Street
Cambridge, MA 02138
(617) 497-2070
Fax: (617) 547-2445
Website: www.advancedmagnetics.com
Employees: 24 in MA
History: Founded in 1981
Ownership: Public: AMEX-AVM
Commercial Market Sectors:
Human Therapeutics
Areas of Research: Anemia, Cancer, Cardiovascular
Products:
Feridex I.V.®: liver contrast agent,
GastroMARK®: oral contrast agent used for delineating

Alantos Pharmaceuticals, Inc.

840 Memorial Drive
Cambridge, MA 02139
(617) 577-0011
Fax: (617) 494-9882
Website: www.alantos.com
Employees: 15 in MA (45 worldwide)
History: Founded in 1999
Facilities: Research Subsidiary in Heidelberg, Germany;
Headquarters in Cambridge, MA
Ownership: Private
Commercial Market Sectors:

Other: Small Molecule Drug Discovery

Alkermes, Inc.

88 Sidney Street
Cambridge, MA 02139
(617) 494-0171
Fax: (617) 494-9263
Website: www.alkermes.com
Employees: 400 in MA (550 worldwide)
History: Founded in 1987
Facilities: manufacturing in Cambridge, MA; Headquarters, Laboratories in Cambridge, MA; Manufacturing in Wilmington, OH; Offices in Cincinatti, OH; Offices in Cambridge, UK; manufacturing in Chelsea, MA
Ownership: Public: NASDAQ-ALKS
Commercial Market Sectors:
Human Therapeutics
Areas of Research: Drug Delivery
Products:
ProLease/Nutropin Depot/pediatric: growth hormone deficiency
Medisorb/Risperdal Consta: schizophrenia
ProLease/Nutropin Depot/adults: growth hormone deficiency
Medisorb/Vivitrex: alcoholism + opiate abuse

Alnylam Pharmaceuticals

790 Memorial Drive
Cambridge, MA 02142
Employees: 1 in MA
Ownership: Private
Commercial Market Sectors:
Human Therapeutics

ALS Therapy Development Foundation

215 1st Street
Cambridge, MA 02142-1221
617-796-8826
Fax: 617-796-9652
Website: www.als.net/alstdf/
Employees:
Ownership: Private
Commercial Market Sectors:
Areas of Research: neurology, immunology, genetics, pharmacology and drug development.

Altus Pharmaceuticals, Inc.

625 Putnam Avenue
Cambridge, MA 02139
(617) 299-2900
Fax: (617) 299-2999
Website: www.altus.com
Employees: 65 in MA
History: Founded in 1992
Facilities: Headquarters, Laboratories in Cambridge, MA
Ownership: Private
Commercial Market Sectors:
Human Therapeutics
Industrial Biology
Platform Technologies
Other: Oral Lumenal Therapies; Drug Delivery
Areas of Research: Pancreatic Insufficiency
Products:
Thera-CLEC (TM)
CLECÂ® Brand Biocatalysts
Custom CLECÂ® Catalysts
Metabolites

Amgen, Inc.

One Kendall Square, Building 1000
Cambridge, MA 02139
(617) 444-5000
Fax: (617) 577-9511
Website: www.amgen.com
Employees: 2100 in MA (20000 worldwide)
History: Founded in 1980
Facilities: Headquarters in Thousand Oaks, CA
Ownership: Public: NASDAQ-AMGN
Commercial Market Sectors:
Human Therapeutics
Areas of Research: Oncology, Nephrology, Rheumatology, Blood Disorders, Bone Marrow Disorders, Infectious Disease, Obesity, Neurodegenerative Diseases, such as Parkinson's Disease and Alzheimer's Disease
Products:
EPOGEN® (Epoetin alfa): stimulates and regulates the production
NEUPOGEN®: a recombinant granulocyte colony-stimula
Keratinocyte growth factor: Cancer
Aranesp
Enbrel
Kepivance
Kineret

Neulasta
Sensipar
Vectibix

Archemix Corporation

300 Third Street
Cambridge, MA 02142
(617) 621-7700
Fax: (617) 621-9300
Website: www.archemix.com
Employees: 24 in MA
History: Founded in 2000
Ownership: Private
Commercial Market Sectors:
Platform Technologies

Ariad Pharmaceuticals, Inc.

26 Landsdowne Street
Cambridge, MA 02139
(617) 494-0400
Fax: (617) 225-2860
Website: www.ariad.com
Employees: 65 in MA
History: Founded in 1991
Facilities: Headquarters, Laboratories in Cambridge, MA
Ownership: Public: NASDAQ-ARIA
Commercial Market Sectors:
Genomics/Proteomics
Human Therapeutics
Areas of Research: Cancer, Osteoporosis

Aveo Pharmaceuticals, Inc. (f/k/a GenPath Pharmaceuticals)

75 Sidney Street, 4th Floor
Cambridge, MA 02139
617-299-5000
Fax: 617-995-4995
Website: www.aveopharma.com
Employees: 67 in MA
Ownership: Private
Company Description:
AVEO employs powerful, proprietary genetic model systems to discover and develop drugs against essential targets critical to the origin, maintenance and spread of malignant tumors. Founded in 2002, the Company has raised approximately $60M in two rounds of

financing from leading life science investors: Flagship Ventures, Greylock Partners, Highland Capital Partners, MPM Capital, Lotus Biosciences, Oxford Bioscience Partners, Prospect Ventures, Venrock Associates, as well as several private investors. Partnering is central to AVEO's business model.

Biogen Idec, Inc.

14 Cambridge Center
Cambridge, MA 02142
(617) 679-2000
Fax: (617) 679-3100
Website: www.biogenidec.com
Employees: 1438 in MA (2352 worldwide)
History: Founded in 1978
Facilities: Headquarters, Labs Manufacturing in Cambridge, MA; Manufacturing, Labs, Office in Research Triangle Park,, NC
Ownership: Public: NASDAQ-BGEN
Commercial Market Sectors:
Human Therapeutics
Areas of Research: Immunology Cancer, Neuroscience, Fibrosis.

Products:
Avonex: Multiple Sclerosis
Antegrew: MS, Chrones
Amevive: Psoriasis
Company Description:
Biogen is a global biotechnology company principally engaged in discovering and developing drugs for human health care through genetic engineering. The world's oldest independent biotechnology company, Biogen was founded in 1978 by a group of internationally acclaimed scientists, including two U.S. academics who would later win Nobel Prizes.

Bionaut Pharmaceuticals

61 Moulton Street
Cambridge, MA 02138
(617) 661-4900
Fax: (617) 661-6888
Website: www.bionautpharma.com
Employees: 5 in MA
History: Founded in 2000
Facilities: Labs + Offices in Boston, MA
Ownership: Private
Commercial Market Sectors:
Human Diagnostics, Human Therapeutics
Areas of Research: Cell-based Assays, Cancer, Inflammation, Metabolic Disease

Biopure Corporation

11 Hurley Street
Cambridge, MA 02141
(617) 234-6500
Fax: (617) 234-6505
Website: www.biopure.com
Employees: 208 in MA
History: Founded in 1984
Ownership: Public: NASDAQ-BPUR
Commercial Market Sectors:
Human Therapeutics, Veterinary Diagnostics/Therapeutics
Areas of Research: Anemia

Products:
OxyglobinÂ®: treatment of anemia in dogs
HemopureÂ®: an oxygen therapeutic

BioTrove, Inc.

620 Memorial Drive
Cambridge, MA 02139
(617) 551-3400
Fax: (617) 551-3401
Website: www.biotrove.com
Employees: 17 in MA
History: Founded in 2000
Facilities: Lab in Cambridge, MA
Ownership: Private
Commercial Market Sectors:
Agricultural Biotechnology
Contract Research
Genomics/Proteomics
Human Diagnostics
Human Therapeutics
Platform Technologies

BioVex, Inc.

245 First Street, Suite 1800
Cambridge, MA 02142
617-444-8445
Fax: 617-444-8405
Website: biovex.com
Employees:
Ownership: Private
Commercial Market Sectors:
Targeted treatments for cancer and the prevention of infectious disease.

Boston Biochem, Inc.

One Kendall Sq, Bldg 600, PMB 319
Cambridge, MA 02139
(617) 241-7072
Fax: (617) 241-7072
Website: www.bostonbiochem.com
Employees: 19 in MA
History: Founded in 1997
Ownership: Private
Commercial Market Sectors:
Contract Manufacturing

Cell NetwoRx LLC

237 Putnam Ave 2nd Floor, Putnam II
Cambridge, MA 02139
617-547-2983
Fax: 617-349-3590
Employees: 2 in MA
History: Founded in 2004
Ownership: Private
Commercial Market Sectors:
Human Therapeutics

Codon Devices

One Kendall Square, Building 700, First Floor
Cambridge, MA 02139
617-995-7999
Fax: 617-995-7970
Website: www.codondevices.com
Employees: 2 in MA
History: Founded in 2004
Ownership: Private
Commercial Market Sectors:
Genomics/Proteomics

CombinatoRx, Inc

245 First Street, Sixteenth Floor
Cambridge, MA 02142
(617) 425-7000
Fax: (617) 425-7010
Website: www.combinatorx.com
Employees: 42 in MA
History: Founded in 2000
Ownership: Private

Commercial Market Sectors:
Bioinformatics Services
Human Therapeutics
Areas of Research: Autoimmune, Cancer, Infectious Disease, Metabolic Disease
Company Description:
CombinatoRx, Inc. is a biopharmaceutical company focused on developing new medicines built from synergistic combinations of approved drugs. CombinatoRx has discovered and advanced into clinical trials a portfolio of seven product candidates targeting multiple immuno-inflammatory diseases and cancer. Founded in 2000 by leading scientists from Harvard and MIT, the company has raised $90M.

Correlagen, Inc.

222 Third Street, Suite 1100
Cambridge, MA 02142
617-577-0152
Website: www.correlagen.com
Employees: 2 in MA
Ownership: Private
Commercial Market Sectors:
Genomics/Proteomics

Curis, Inc.

45 Moulton Street
Cambridge, MA 02138-1118
(617) 503-6515
Fax: (617) 503-6501
Website: www.curis.com
Employees: 155 in MA
History: Founded in 2000
Facilities: Headquarters in Cambridge, MA; Manufacturing in Cambridge, MA; Labs in Cambridge, MA
Ownership: Public: NASDAQ-CRIS
Commercial Market Sectors:
Human Therapeutics
Areas of Research: Neurological, Oncology, Angiogenesis, Diabetes
Products:
Chondrogel: Vesicoureteral Reflux
OP-1: Bone growth
Company Description:
Curis, Inc. was formed through the merger of Creative BioMolecules, Inc., Ontogeny, Inc. and Reprogenesis Inc.

Domantis, Ltd.

58 Charles Street, Suite 303
Cambridge, MA 02141
617-267-4793
Fax: 253-595-8585
Website: www.domantis.com
Employees: 20 in MA
History: Founded in 2001
Ownership: Private
Commercial Market Sectors:
Genomics/Proteomics
Company Description:
Domantis, formerly Diversys, Inc., is a biotechnology company developing a range of technologies for the in vitro evolution and engineering of recombinant proteins. Established by Ian Tomlinson and Greg Winter in partnership with the UK Medical Research Council and a London-based venture capital group, Medical Venture Management Limited.

Dyax Corporation

One Kendall Square, Bldg. 600, Suite 623
Cambridge, MA 02139
(617) 225-2500
Fax: (617) 225-2501
Website: www.dyax.com
Employees: 100 in MA (220 worldwide)
History: Founded in 1995
Facilities: Headquarters/Labs in Cambridge, MA
Ownership: Public: NASDAQ-DYAX
Commercial Market Sectors:
Human Diagnostics, Human Therapeutics, Platform Technologies
Areas of Research: Cancer, Inflammation/Autoimmune

Elixir Pharmaceuticals, Inc.

1 Broadway Street, Suite 600
Cambridge, MA 02142
(617) 621-1599
Fax: (617) 621-1510
Website: www.elixirpharm.com
Employees: 8 in MA
History: Founded in 1999
Ownership: Private
Commercial Market Sectors:
Human Therapeutics
Areas of Research: Aging

Ensemble Discovery Corporation

99 Erie Street
Cambridge, MA 02139
617-492-6977
Fax: 617-492-6689
Employees: (5 worldwide)
Ownership: Private
Commercial Market Sectors:
Human Therapeutics
Company Description:
Ensemble Discovery Corporation is developing a novel approach to chemical discovery based on a highly integrated set of processes that combine chemistry, biology and nanotechnology. Central to its approach is DNA Programmed Chemistry (DPC), an innovative method for chemical synthesis based on the groundbreaking work of Professor David Liu of Harvard University.

EnVivo Pharmaceuticals, Inc.

790 Memorial Drive, Suite 102
Cambridge, MA 02139
(617) 374-3777
Fax: (617) 374-9337
Website: www.envivopharma.com
Employees: 5 in MA
History: Founded in 2001
Ownership: Private
Commercial Market Sectors:
Human Therapeutics
Areas of Research: Central Nervous System (CNS) Disorders, Alzheimer's, Parkinson's

ETEX Corporation

350 Massachusetts Avenue
Cambridge, MA 02139
(617) 577-7270
Fax: (617) 577-7170
Website: www.etexcorp.com
Employees: 43 in MA
History: Founded in 1989
Ownership: Private
Commercial Market Sectors:
Human Therapeutics
Areas of Research: Damaged and Diseased Bone

FoldRx

300 Technology Square, 5th Floor
Cambridge, MA 02139
(617) 252-5500
Fax: (617) 252-5501
Website: foldrx.com
Employees: 3 in MA
History: Founded in 2003
Ownership: Private
Commercial Market Sectors:
Genomics/Proteomics, Human Therapeutics
Company Description:
FoldRx was formed in 2003 based on technology licensed from the Whitehead Institute at MIT and the Scripps Research Institute.

Galenea

300 Technology Square, 2nd Floor
Cambridge, MA 02139
617-374-1010
Fax: 775-249-4463
Website: www.galenea.com
Employees: 5 in MA
Ownership: Private

Genetic Services, Inc.

One Kendall Square Building 300
Cambridge, MA 02142
617-252-9100
Fax: 617-252-9119
Website: www.geneticservices.com
Ownership: Private

Genetix Pharmaceuticals, Inc.

840 Memorial Drive
Cambridge, MA 02139
(617) 491-5601
Fax: (617) 576-2421
Website: www.genetixpharm.com
Employees: 12 in MA
History: Founded in 1992
Facilities: Headquarters + R+D in Cambridge, MA
Ownership: Private
Commercial Market Sectors:

Human Therapeutics
Areas of Research: Cancer

Genfit Corp.

245 First Street, 18th Floor, Suite 1806
Cambridge, MA 02142
(617) 444-8416
Fax: (617) 444-8405
Website: www.genfit.com
Employees: 1 in MA (2 worldwide)
Ownership: Private
Commercial Market Sectors:
Genomics/Proteomics, Bioinformatics Services, Human Therapeutics

Genstruct, Inc.

One Alewife Center Suite 100
Cambridge, MA 02140
617-547-5421
Fax: 617-547-5442
Website: www.genstruct.com
Ownership: Private

Genzyme Corporation

One Kendall Square
Cambridge, MA 02139-1562
(617) 252-7570
Fax: (617) 374-7368
Website: www.genzyme.com
Employees: 4989 in MA (5864 worldwide)
History: Founded in 1981
Facilities: Headquarters in Cambridge, MA; Office in CERGY-PONTOISE CEDEX, FRANCE; Manufacturing in Waterford, Ireland; Headquarters in Framingham, MA; Manufacturing in Allston, MA; Manufacturing in Liestal, Switzerland
Ownership: Public: NYSE-GENZ
Commercial Market Sectors:
Biological Devices
Human Diagnostics
Human Therapeutics
Other: Biotechnoloy/Biopharmaceutical Products
Areas of Research: Rare Genetic Diseases, Cancer, Cardiothoracic, Orthopedics.
Products:
FocalSeal: prevents leaks after surgery
Seprafilm/Sepramesh: adhesion prevention
Synvisc: treats osteoarthritis of the knee

WelChol: LDl cholesterol lowering agent
Epicel: treatment for severe burn injuries
Renagel: end-stage renal disease
Thyrogen: Thyroid cancer
Cerezyme: Type 1 Gaucher Disease
Carticel: treatment for knee cartilage damage

Gloucester Pharmaceuticals

One Broadway, 14th Floor
Cambridge, MA 02142
617-583-1300
Fax: 617-5831368
Website: www.gloucesterpharma.com
Employees: (4 worldwide)
Ownership: Private
Commercial Market Sectors:
Human Therapeutics

Gwathmey Inc.

763 Concord Avenue, Bldg. E
Cambridge, MA 02138
(617) 491-0022x107
Fax: (617) 492-5545
Website: www.gwathmey.com
Employees: 17 in MA
History: Founded in 1996
Facilities: Animal Housing in Cambridge, MA; HQ, Labs in Cambridge, MA
Ownership: Private
Commercial Market Sectors:
Contract Research, Genomics/Proteomics, Platform Technologies
Areas of Research: Autoimmune, Cancer, Cardiovascular, Oncology, Inflammation, Arthritis, Infectious Disease, CNS, Diabetes, Metabolic

Hydra Biosciences

790 Memorial Drive, Suite 203
Cambridge, MA 02139
(617) 494-5230
Fax: (617) 494-5245
Website: www.hydrabiosciences.com
Employees: 19 in MA
History: Founded in 2001
Ownership: Private
Commercial Market Sectors:
Other: Biopharmaceutical

Areas of Research: Molecular Regeneration

Idenix Pharmaceuticals, Inc.

One Kendall Square, Bldg 1400
Cambridge, MA 02139
(617) 995-9800
Fax: (617) 995-9801
Website: www.idenix.com
Employees: 45 in MA (80 worldwide)
History: Founded in 1998
Facilities: Chemistry Lab in Montpellier France; Virology/Pharmac Lab in Cambridge, MA; Biology Lab in Cagliari, Italy; Headquarters in Cambridge, MA
Ownership: Private
Commercial Market Sectors:
Human Therapeutics
Areas of Research: Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), HIV

Idera Pharmaceuticals

345 Vassar Street
Cambridge, MA 02139
(617) 679-5500
Fax: (617) 679-5592
Website: www.iderapharma.com
Employees: 20 in MA
History: Founded in 1989
Facilities: Office + Laboratory in Cambridge, MA
Ownership: Public: AMEX: IDP-IDP
Commercial Market Sectors:
Human Therapeutics, Platform Technologies
Areas of Research: Cancer, Infectious Diseases, Immune Modulation.

ImmunoGen, Inc.

128 Sidney Street
Cambridge, MA 02139
(617) 995-2500
Fax: (617) 995-2510
Website: www.immunogen.com
Employees: 94 in MA
History: Founded in 1981
Facilities: Manufacturing in Norwood, MA; Lab in Cambridge, MA
Ownership: Public: NASDAQ-IMGN
Commercial Market Sectors:
Human Therapeutics
Areas of Research: Cancer

Infinity Pharmaceuticals, Inc.

780 Memorial Drive
Cambridge, MA 02139
(617) 453-1000
Fax: (617) 453-1001
Website: www.infinitypharm.com
Employees: 80 in MA
History: Founded in 2001
Facilities: Lab/office in Boston, MA
Ownership: Private
Commercial Market Sectors:
Human Therapeutics

Intelligent Medical Devices, Inc.

58 Charles Street
Cambridge, MA 02141
617-871-6400
Fax: 617-871-6399
Website: www.intelligentmd.com
Ownership: Private
Company Description:
Intelligent Medical Devices (IMD) is developing point-of-care medical devices to aid in patient diagnosis and provide treatment guidance.

Javelin Pharmaceuticals, Inc.

125 Cambridgepark Drive
Cambridge, MA 02140
617-349-4500
Fax: 617-349-4505
Website: www.javelinpharmaceuticals.com
Employees: 6 in MA (15 worldwide)
History: Founded in 2005
Ownership: Public
Commercial Market Sectors:
Other: Speciality Pharma

Kard Scientific

955 Massachusetts Avenue, #305
Cambridge, MA 02139
978-658-4125
Fax: 978-658-6564
Website: www.KardScientific.com
Employees: (7 worldwide)
History: Founded in 2002

Ownership: Private
Commercial Market Sectors:
Agricultural Biotechnology

Keel Pharmaceuticals

215 First Street, Suite 104
Cambridge, MA 02142
617-225-0834
Fax: 617-225-0835
Website: www.keelpharmaceuticals.com
Employees: 3 in MA
History: Founded in 2002
Ownership: Private
Commercial Market Sectors:
Human Therapeutics

Link Medicine Corporation

790 Memorial Drive
Cambridge, MA 02139
617-374-4776
Employees: 3 in MA
History: Founded in 2005
Ownership: Private
Commercial Market Sectors:
Human Therapeutics

Company Description:
Link Medicine was founded by Peter Lansbury (Professor of Neurology, Harvard Medical School; Director, Morris K. Udall Parkinson's Disease Research Center of Excellence at Brigham and Women's Hospital) to accelerate the development of medicines that slow the progression of Parkinson's Disease.

Magen BioSciences

790 Memorial Drive, Suite 200B,
Cambridge, MA 02139
617-494-8732
Fax: 617-494-8752
Website: www.magenbiosciences.com
Employees: 2 in MA
History: Founded in 2006
Ownership: Private
Commercial Market Sectors:
Human Therapeutics

Merrimack Pharmaceuticals, Inc.

101 Binney Street
Cambridge, MA 02142
(617) 441-1000
Fax: (617) 491-1386
Website: www.merrimackpharma.com
Employees: 24 in MA
History: Founded in 2000
Facilities: Headquarters in Cambridge, MA; Labs in Cambridge, MA
Ownership: Private
Commercial Market Sectors:
Genomics/Proteomics, Human Therapeutics
Areas of Research: Cancer and autoimmune diseases, specifically rheumatoid arthritis and multiple sclerosis.
Company Description:
Founded by leading scientists from MIT and Harvard, the company's proprietary Network Biology discovery platform enables the high throughput profiling of protein networks as a basis for improved validation, lead identification and speed in the development of innovative, effective and safe therapeutics.

Mersana Therapeutics

840 Memorial Drive
Cambridge, MA 02139
617-498-0020
Fax: 617-498-0109
Website: www.mersana.com
Employees: 4 in MA
Ownership: Private
Commercial Market Sectors:
Human Therapeutics
Company Description:
Mersana Therapeutics is an oncology company developing new therapeutics based on powerful glycomimetic technologies invented at the Massachusetts General Hospital (MGH) (Boston, MA).

Metabolix, Inc.

303 Third Street
Cambridge, MA 02142

(617) 492-0505
Fax: (617) 492-1996
Website: www.metabolix.com
Employees: 29 in MA
History: Founded in 1993
Facilities: Headquarters in Cambridge, MA

Ownership: Private
Commercial Market Sectors:
Agricultural Biotechnology
Areas of Research: Biopolymers

Microbia, Inc.

320 Bent Street
Cambridge, MA 02142
(617) 621-7722
Fax: (617) 494-0908
Website: www.microbia.com
Employees: 63 in MA
History: Founded in 1998
Facilities: Headquarters in Cambridge, MA
Ownership: Private
Commercial Market Sectors:
Human Therapeutics
Areas of Research: Anti-Infectives

Millennium Pharmaceuticals, Inc.

75 Sidney Street
Cambridge, MA 02139
(617) 679-7000
Fax: (617) 679-7780
Website: www.mlnm.com
Employees: 1400 in MA (2025 worldwide)
History: Founded in 1993
Facilities: Research Facility in San Francisco, CA; Research Facility in Cambridge, UK; HQ + Research Facility in Cambridge, MA; Business Office in Tokyo, Japan; Business Office in Tel Aviv, Isreal
Ownership: Public: NASDAQ-MLNM
Commercial Market Sectors:
Genomics/Proteomics
Areas of Research: Metabolic Diseases, Cardiovascular Diseases, Oncology, Inflamation.
Products:
Integrilin (eptifibatide)
Campath (alemtuzumab)

Modular Genetics, Inc.

325 Vassar St.
Cambridge, MA 02139

617 441 6000
Fax: 617 441 6001
Website: www.modulargenetics.com
Employees: 6 in MA
History: Founded in 2000
Ownership: Private
Commercial Market Sectors:
Platform Technologies
Other: Gene Engineering

Molecular Insight Pharmaceuticals, Inc.

160 Second Street
Cambridge, MA 02142
(617) 492-5554
Fax: (617) 492-5664
Website: www.molecularinsight.com
Employees: 12 in MA
History: Founded in 1997
Ownership: Private
Commercial Market Sectors:
Human Diagnostics, Platform Technologies
Areas of Research: Cardiovascular Disease, Oncology, Neurological Disorders, Infectious Diseases
Products:
BIO-110 (BMIPP): cardiac imaging agent

Momenta Pharmaceuticals, Inc.

43 Moulton Street
Cambridge, MA 02138
(617) 491-9700
Fax: (617) 876-8012
Website: www.momentapharma.com
Employees: 28 in MA
History: Founded in 2002
Ownership: Private
Commercial Market Sectors:
Human Therapeutics
Other: Glycomics

Novartis Institutes for BioMedical Research, Inc.

400 Technology Square, 7th Floor
Cambridge, MA 02139
617-871-8000
Fax: 617-551-9540

Website: www.nibr.novartis.com
Ownership: Public
Commercial Market Sectors:
Other: Pharmaceutical Research
Company Description:
Novartis Institutes' Cambridge facilities encompass 750,000 square feet of laboratory and office space. Research in cardiovascular disease, oncology, infectious disease, diabetes, ophthalmology and skeletal muscle disease is headquartered in Cambridge. In addition, Cambridge is home to the following platform technologies: Global Discovery Chemistry, Functional Genomics, Developmental & Molecular Pathways, and Models of Disease Center.

NovoBiotic Pharmaceuticals

767C Concord Avenue
Cambridge, MA 02138
617-864-2880
Website: www.novobiotic.com
Employees: 5 in MA
Ownership: Private
Commercial Market Sectors:
Human Therapeutics

OmniGene Bioproducts, Inc.

763 D Concord Avenue
Cambridge, MA 02138
(617) 576-1966
Fax: (617) 547-9256
Employees: 11 in MA
History: Founded in 1995
Facilities: Research Laboratory Offices in Cambridge, MA
Ownership: Private
Commercial Market Sectors:
Contract Research, Industrial Biology, Platform Technologies
Areas of Research: Fine Chemicals (Vitamins, Amino Acids) Production, Enzyme Production, Antibacterial Targets.

One Cell Systems, Inc.

100 Inman Street
Cambridge, MA 02139
(617) 868-2399
Fax: (617) 492-7921
Website: www.onecell.com
Employees: 10 in MA
History: Founded in 1992

Ownership: Private
Commercial Market Sectors:
Agricultural Biotechnology, Genomics/Proteomics, Human Diagnostics

Organon Research Center USA

245 First Street, 6th Floor
Cambridge, MA 02142
617-374 5303
Fax: fax (617)577 0470
Website: www.organon.com
Employees: (10 worldwide)
Ownership: Public
Commercial Market Sectors:
Human Therapeutics
Products:
Folistim

Oxxon Therapeutics Inc.

185 Alewife Brook Parkway Suite 410
Cambridge, MA 02138
617-383-2100
Fax: 617-383-2107
Website: www.oxti.com
Employees: 3 in MA
Ownership: Private
Commercial Market Sectors:
Human Therapeutics

Peptimmune, Inc.

64 Sidney Street, Suite 380
Cambridge, MA 02139
617-591-5555
Fax: 617-661-8855
Website: www.peptimmune.com
Employees: 16 in MA
History: Founded in 2003
Ownership: Private
Commercial Market Sectors:
Human Therapeutics
Company Description:
Peptimmune, Inc. is a privately held clinical stage biotechnology company focused on advancing both novel and proven therapies for autoimmune and metabolic diseases through the development of second generation therapeutics. Peptimmune was spun-off from Genzyme Corporation in 2003.

Percivia, LLC.

1 Hampshire Street
Cambridge, MA 02139
Employees: (11 worldwide)
Ownership: Private
Commercial Market Sectors:
Human Therapeutics

Pervasis Therapeutics, Inc.

One Kendall Square, Building 600, 2nd Floor
Cambridge, MA 02139
617-621-3407
Fax: 617-621-3408
Website: www.pervasistx.com
Employees: 7 in MA
History: Founded in 2003
Ownership: Private
Commercial Market Sectors:
Biological Devices

Pfizer Research Technology Center

620 Memorial Drive
Cambridge, MA 02139
(617) 551-3000
Fax: (617) 551-3347
Website: www.pfizerdtc.com
Employees: 70 in MA (90000 worldwide)
History: Founded in 1849
Facilities: Headquarters in New York, NY
Ownership: Public: NYSE-PFE
Commercial Market Sectors:
Human Therapeutics, Veterinary Diagnostics/Therapeutics
Areas of Research: Diabetes, Cardiovascular Diseases, Infectious Diseases, Allergy
Company Description:
Founded in 1999, the RTC is a small, vibrant, and fully functional PGRD site. The mission of the RTC is to apply cutting edge technologies to address specific challenges that prevent patients from receiving the innovative medicines they need. Located near several leading institutions, including Harvard University, the Massachusetts Institute of Technology (MIT), the Whitehead Institute and Harvard Medical School, the RTC fosters a unique culture that prizes innovation, creativity and risk-taking in research.
Products:
Procardia XL: Cardiovascular Diseases
Cardura: Cardiovascular Diseases
Accupril/Accuretic: Cardiovascular Diseases
Neurontin: Central Nervous System Disorders

Zithromax: Infectious Diseases
Viracept: Infectious Diseases
Diflucan: Infectious Diseases
Zoloft: Central Nervous System Disorders
Zyrtex: Allergy
Norvasc: Cardiovascular Diseases
Lipitor: Cardiovascular Diseases
Glucotrol XL: Diabetes
Viagra: Erectile Dysfunction

PharmaMar USA Inc.

64 Sidney Street
Cambridge, MA 02139
617-868-3797
Fax: 617-868-0109
Website: www.pharmamar.com
Ownership: Public
Commercial Market Sectors:
Human Therapeutics

Phylonix Pharmaceuticals, Inc.

100 Inman Street
Cambridge, MA 02139
617-441-6700
Fax: 617-441-6766
Website: www.phylonix.com
Employees: 20 in MA
History: Founded in 1997
Ownership: Private
Commercial Market Sectors:
Platform Technologies

Pulmatrix Inc.

12 Emily Street
Cambridge, MA 02139
617-497-6789
Fax: 617-497-6790
Website: www.pulmatrix.com
Employees: 4 in MA (5 worldwide)
History: Founded in 2003
Ownership: Private
Commercial Market Sectors:
Human Therapeutics

Radius

300 Technology Square, 5th Floor
Cambridge, MA 02139
(617) 551-4700
Fax: (617) 551-4701
Website: www.radiuspharm.com
Employees: 8 in MA
Ownership: Private
Commercial Market Sectors:
Human Therapeutics

Sanofi Aventis Pharmaceuticals, Cambridge Genomics Center

26 Landsdowne Street
Cambridge, MA 02139
(617) 768-4127
Fax: (617) 374-8811
Website: www.sanofi-aventis.com
Employees: 56 in MA
History: Founded in 2000
Facilities: Genomics Research in Cambridge, MA
Ownership: Public: EUROPE-AVE
Commercial Market Sectors:
Genomics/Proteomics
Areas of Research: Respiratory, Cardiocascular, Oncology, Diabetes
Products:
Nasacort: Allergies
Allegra: Allergies
Lantus: Diabetes
Taxotere: Oncology
Lovenox: Heart attacks

Saoirse Corporation

300 Technology Square
Cambridge, MA 02139
617-250-5910
Fax: 617-497-1581
Website: www.saoirse.com
Employees: 19 in MA
Ownership: Private
Commercial Market Sectors:
Human Therapeutics
Company Description:
Nanosystem Based Biological Technology. Founded by Patrick Kane, an MIT Student.

Schering-Plough Research Institute - Cambridge

840 Memorial Drive
Cambridge, MA 02139
617-868-1500
Fax: 617-868-1515
Website: www.schering-plough.com
Employees: 87 in MA
Ownership: Public
Commercial Market Sectors:
Genomics/Proteomics
Bioinformatics Services
Human Therapeutics
Company Description:
Schering-Plough Research Institute, Cambridge, MA (formerly NeoGenesis Pharmaceuticals) combines the expertise and benefits of a global pharmaceutical company with an intimate and entrepreneurial biotechnology environment in Cambridge. The site is applying novel drug discovery technologies such as, ALIS (Automated Ligand Identification System) and high throughput Chemical technologies, towards discovery of drug candidates in various disease areas, such as cancer, metabolic diseases, infection and CNS disorders.

Since arriving in January 2006, Schering-Plough Research Institute has doubled in size, leasing almost an entire building. The New Jersey-based drug research and development company on June 30 signed a lease for another 64,000 square feet at 320 Bent St., bringing the total amount of lab space leased to about 135,000 square feet. Last November, the institute, the research arm of Schering-Plough Corp. (NYSE: SGP), signed a lease for about 71,000 square feet with the building's owner, Lyme Properties.

Shire Pharmaceuticals

700 Main Street
Cambridge, MA 02139
617-349-0200
Fax: 617-613-4005
Website: www.shire.com
Employees: 370 in MA (410 worldwide)
History: Founded in 1997
Ownership: Public
Commercial Market Sectors:
Human Therapeutics
Company Description:
Shire's global headquarters are located in Basingstoke, UK, and North American headquarters are located in suburban Philadelphia, PA (Wayne). Shire has significant operations in Cambridge, Massachusetts and Owings Mills, MD, as well as in the world

key pharmaceutical markets (US, Canada, UK, France, Italy, Spain and Germany), in addition to a specialist drug delivery unit in the US.

Products:
Replagel

Sirtris Pharmaceuticals

790 Memorial Drive, Suite 104
Cambridge, MA 02139
617-252-6920
Fax: 617-252-6924
Website: www.sirtrispharma.com
Employees: (5 worldwide)
History: Founded in 2004
Ownership: Private
Commercial Market Sectors:
Human Therapeutics
Company Description:
Sirtris Pharmaceuticals is a biopharmaceutical company developing and commercializing novel therapeutics that modulate sirtuins. Sirtris Pharmaceuticals was founded by Rich Aldrich, Richard Pops, Paul Schimmel, David Sinclair and Christoph Westphal, and has raised a total of $82 million since inception. Its investors include Polaris Venture Partners, TVM Capital, Cardinal Partners, Skyline Ventures, Three Arch Partners, The Wellcome Trust, Bessemer Venture Partners, Novartis Bioventures Fund, Cargill Ventures, Genzyme Ventures, QVT Fund LP, Cycad Group, Hunt Ventures, Red Abbey, and Alexandria Real Estate Equities, Inc.

SolMap Pharmaceuticals, Inc.

196 Broadway 2nd Flr
Cambridge, MA 02139
617-250-7020
Fax: 617-250-7021
Website: www.solmap-pharma.com
Employees: 5 in MA
History: Founded in 2005
Ownership: Private
Commercial Market Sectors:
Contract Research
Bioinformatics Services
Other: Drug Discovery
Company Description:
SolMap Pharmaceuticals Inc. was founded as a spinoff from the Structural Bioinformatics Laboratory of Dr. Sandor Vajda at Boston University.

Tepha, Inc

840 Memorial Drive
Cambridge, MA 02139
617-995-5400
Fax: 617-995-5401
Website: www.tepha.com
Employees: 7 in MA
History: Founded in 1998
Ownership: Private
Commercial Market Sectors:
Biological Devices
Company Description:

Therion Biologics Corp.

76 Rogers Street
Cambridge, MA 02142
(617) 876-7779
Fax: (617) 876-9391
Website: www.therionbio.com
Employees: 70 in MA
History: Founded in 1991
Facilities: HQ + Lab in Cambridge, MA
Ownership: Private
Commercial Market Sectors:
Human Therapeutics
Areas of Research: Cancer, AIDS

TolerRx Inc.

300 Technology Square, 4th Floor
Cambridge, MA 02139
(617) 354-8100
Fax: (617) 354-8300
Website: www.tolerrx.com
Employees: 27 in MA
History: Founded in 2000
Facilities: Headquarters and Labs in Cambridge, MA
Ownership: Private
Commercial Market Sectors:
Human Therapeutics
Platform Technologies
Areas of Research: Auto Immune, Transplantation, Antibody Technology

TransMolecular, Inc.

840 Memorial Drive 2nd Floor
Cambridge, MA 02139
617-995-3050
Fax: 617-995-3049
Website: www.transmolecular.com
Ownership: Private
Commercial Market Sectors:
Company Description:
TransMolecular, Inc. is a therapeutics biotechnology company committed to discovering, developing and commercializing novel and proprietary drugs to diagnose and treat human diseases having inadequate pharmaceutical alternatives. The Company focuses its drug research on cancer.

Vertex Pharmaceuticals Inc.

130 Waverly Street
Cambridge, MA 02139
(617) 444-6000
Fax: (617) 444-6680
Website: www.vpharm.com
Employees: 558 in MA (1000 worldwide)
History: Founded in 1989
Facilities: PanVera Corporation, a Vertex Subsidiary in Madison, WI; Aurora Biosciences Corporation, a Vertex Subsidiary in San Diego, CA; Vertex Pharmaceuticals Incorporated in Cambridge, MA; Vertex Pharmaceuticals (Europe) Limited in Oxfordshire, UK
Ownership: Public: NASDAQ-VRTX
Commercial Market Sectors:
Genomics/Proteomics
Human Therapeutics
Areas of Research: Viral Diseases, Inflammation, Cancer, Autoimmune Diseases, Neurological Disorders, Genetic Disorders
Products:
AgeneraseÂ®: HIV protease inhibitor

ViaCell, Inc.

245 First Street 15th Floor
Cambridge, MA 02142
(617) 914-3400
Fax: (617) 914-3855
Website: www.viacell.com
Employees: 117 in MA (141 worldwide)
History: Founded in 2000
Facilities: Lab in Worcester, MA; Lab in Singapore; Headquarters in Boston, MA; Lab

in Cambridge, MA
Ownership: Private
Commercial Market Sectors:
Human Therapeutics
Other: Cellular Therapies
Areas of Research: Stem Cell Amplification

Company Description:
ViaCell is a biotechnology company focused on enabling the widespread use of human cells as medicine. ViaCell is headquartered in Cambridge, Massachusetts with a processing and storage facility in Kentucky and additional research and development operations in Singapore.

WMR Biomedical, Inc.

790 Memorial Drive
Cambridge, MA 02139
617-621-1038
Fax: 617-577-0679
Employees: 10 in MA
History: Founded in 2005
Ownership: Private
Commercial Market Sectors:
Biological Devices, Human Therapeutics
Company Description:
Our company, WMR Biomedical, Inc., is a Boston-based medical device company whose scientific founders include George Whitesides and Bob Langer. WMR Biomedical utilizes its expertise in organic and polymer chemistry, material science, biophysics, microfluidics, self-assembly, micro- and nanotechnology, cell-surface biochemistry and drug delivery for the development of new medical devices.

Wyeth Biotech and Wyeth Research Headquarters

87 Cambridge Park Drive
Cambridge, MA 02140
(978)247-9214
Fax: (978)247-3420
Website: www.wyeth.com
Employees: 2581 in MA (52000 worldwide)
History: Founded in 1980
Facilities: Labs in Cambridge, MA; Manufacturing in Andover, MA; Labs in Andover, MA
Ownership: Public: NYSE-AHP
Commercial Market Sectors:
Biological Devices
Human Therapeutics
Areas of Research: Auto Immune, Musculoskeletal, Metabolic and Respiratory Diseases, Infectious Diseases, Neuroscience, Hemophilia

Company Description:
Wyeth has two Massachusetts locations: Wyeth BioPharma Biotech (1 Burtt Road, Andover, MA 01810, 978-475-9214) and Wyeth Research (87 CambridgePark Drive, Cambridge, MA 02140, 617-876-1170). Wyeth is a research-based, global pharmaceutical company responsible for the discovery and development of some of today's most innovative medicines.
Products:
BeneFIX
Indux
ReFacto
Neumega

Xanthus Pharmaceuticals, Inc.

300 Technology Square
Cambridge, MA 02139
(617) 225-0522
Fax: (617) 225-0525
Website: www.xanthus.com
Employees: 28 in MA
History: Founded in 2001
Ownership: Private
Commercial Market Sectors:
Human Therapeutics
Other: Drug Development with Customized Dosing, Oncology
Areas of Research: Cancer

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Interviewees

Dana Mead, Board Member, Pfizer and Head of MIT Corporation

Jonathan King, Professor, MIT

Glen Camiso, BRA Biotechnology and Life Sciences Specialist and Consultant, Boston Consulting Group

Elliott Hillback, Genzyme's Senior Vice President for Corporate Affairs

Anonymous Interviewee

Andrea Schievella, MIT Technology Licensing Office

Charles Cooney, Professor, MIT

Estella Johnson, Cambridge City Government's Community Economic Development Department

Thomas Finneran, former head of Massachusetts Biotechnology Council

Robert Langer, Professor, MIT

Robert Anderson, CFO and VP of Idera

Edward Freedman, Ensembly Discovery Corporation, General Counsel and Vice-President of Operations and Finance