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AUTHOR'S NOTE

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Introduction

- ¹ This paper analyzes the development of the biotechnology industry in New Haven, Connecticut. In 1993 there were only five biotechnology companies in Connecticut. However, by 2004 the state was home to forty-nine biotechnology and pharmaceutical companies. What led to this increase? Through extensive field work, this research makes clear that the most important influence on the development of this cluster was that of Yale University¹. Other contributing factors include the roles played by the state of Connecticut, the city of New Haven, and the local pharmaceutical companies. However, there is little doubt that the dominant influence was the change in attitude and policies of Yale towards biotechnology-based industrial growth, which took place after 1993. As such, the case confirms that universities can have an important impact on local industrial and economic development.
- ² The second part of the paper examines the region prior to 1993. The analysis demonstrates that the region had many of the resources with which industrial clusters were created in other parts of the world (Piore and Sabel, 1984; Porter, 1990; Markusen, 1996). The third part of the paper examines how and why the acceleration in

the development of the biotechnology cluster occurred. The last part of the paper describes the industry as it exists today.

I. – The region prior to the transition

I.1. The Region – Connecticut and the New Haven Metropolitan Area

- 3 Connecticut is situated on the northeast coast of the United States, bordering Massachusetts, Rhode Island, and New York. Its population is roughly 3.4 million, according to the 2000 U.S. Official Census.

Figure I - Connecticut County Map.

The study's region is the New Haven metropolitan area, which includes New Haven and Fairfield Counties in Connecticut

Source : (State of Connecticut, 2005).

- 4 New Haven is located about an hour and a half and 80 miles from New York City, and about two and a half hours and 137 miles from Boston, Massachusetts. There are no direct flights to New Haven, and the local airport provides only flights to Philadelphia. According to the 2000 census, the total population of the New Haven metropolitan area, seen in figure 1, is about 1.7 million, divided between New Haven County (population 824,000) and Fairfield County (882,567). The city of New Haven's population of 119,491 is composed of 43.5 % whites, 37.4 % African American, 0.4 % Asians, 3.9 % Native Hawaiian and other Pacific Islanders, and 0.1 % other races. The New Haven metropolitan area is home to seven institutions of higher learning, which provide access to cutting-edge research in critical areas such as medicine, information technology, biotechnology, and architecture. The most notable of New Haven's institutions is Yale University, the third-oldest institution of higher learning in America.
- 5 Despite its location, size, and history, the city has experienced problems similar to much larger US cities. The city's crime rate in the 1990s was higher than the US national averages, specifically in the Hills, Science Park, and by the Boulevard

neighbourhoods. In 1994, New Haven was described as « a war zone of poverty, crime and drugs, as frightening as any city in America » (Sedgwick, 1994). The sense of crisis about the city was growing in the 1980s. For example, thirty-four people were killed in New Haven in 1989, the city's highest murder rate in recent history. Fuelled by the crack cocaine trade, rival gangs fought violent turf battles all over the city (Ball, 1999). Safety and security were particular issues for local high-tech firms when considering to locate in the city centre. Seemingly small issues, such as street lighting, provision of sidewalks, employee safety, and parking became important factors in their decisions to remain in the city.

1.2. Yale University in the mid 1990's

- 6 Yale University, one of the world's leading research universities, is known for its excellence in many fields, including life sciences. However, its culture of non-involvement in the community in general and with industry in particular created a situation in which it failed to reap the credit for several important discoveries, such as the transgenic mouse. For many years Yale was not active in technology transfer and by 1993 had spun out only three biotechnology companies. This attitude of non-involvement in industry changed in the period of 1993-1996. In order to demonstrate this change, this section examines the university finances, faculty, student enrollment, and university policies with regards to IP and technology transfer, as well as regional economic development before 1993. This analysis proves that while Yale's resources have hardly changed over the years, its attitude towards applied research and technology transfer created the fundamental difference in the local economy.
- 7 Yale was not a promoter of applicable research or of working with industry. Hence, in 1994, Yale spent \$224,939,000 on research and development (R&D) and registered only 16 patents. It is interesting to compare these figures with MIT, which spent \$ 374,768,000 on R&D in that year and registered 99 patents (National Science Foundation, 2003). While Yale spent \$ 14,058, 388 per patent MIT spent \$ 3,785,535 per patent. These figures show that MIT produces more patents per research dollar. Also, until 1993, compared to MIT that spun out 30 biotech companies at the time, Yale spun out three companies, only one, Alexion Pharmaceuticals, stayed in the region. These figures are broadly consistent with the reputation of Yale at that time as an institution that was only peripherally and sporadically involved with the local economy and community. As Yale's president Richard Levin noted years later :

Outsiders have long regarded the presence of Yale as one of the city's major assets, but, except for episodic engagement, the University's contributions to the community did not derive from an active, conscious strategy of urban citizenship. It is true that our students, for more than a century, have played a highly constructive role as volunteers. Even a decade ago, two thousand students volunteered regularly in schools, community centers, churches, soup kitchens, and homeless shelters, but these volunteer efforts were neither coordinated nor well supported institutionally. When I became president, in 1993, there was much to be done to transform Yale into an active, contributing institutional citizen... In prior years, however, the university had taken a relatively passive attitude toward the commercialization of its science and technology
(Yale Office of Public Affairs, 2003).
- 8 With the exception of a few departments such as pharmacology, Yale faculty members were not encouraged to work on research with practical applications during this

period. It was actually implied that the outcome of such involvement would have an unfavorable impact on one's academic career. As one interviewee who served on Yale faculty during the late 1960s observed, « One of the things that depressed me was that they did not want to do any application. You could consult but that was not a good status ». Important discoveries were made at Yale during that period, but the Office of Cooperative Research had a somewhat passive view towards commercialization, and only a few discoveries were patented². According to another interviewee :

« There was » very little applied research in Biology, maybe in the medical school or Pharmacology Chemistry departments. In the Biology department it was looked down upon. For example we made the first transgenic mouse and the « Office of Cooperative Research » considered that not to be worthwhile in terms of invention. Yale was very conservative for many years. Not a very active program. Yale actually lost a lot of intellectual property because of this culture. They did not patent on time
(Interview with Yale faculty).

I.3. Local Industry

- 9 Although only a few biotechnology firms established themselves prior to 1993, this was not due to an inhospitable environment. In fact, by 1993, Connecticut was host to five pharmaceutical companies : Pfizer, Bristol-Myers-Squibb, Purdue, Bayer, and Boehringer Ingelheim. Most of these companies had a major presence in the state, including research facilities ; four of these companies are located in the New Haven Metropolitan Area. In 1995, a total of \$ 1.2 billion was spent on pharmaceutical R&D in Connecticut itself (6 % of the nation's total). The companies operated research oriented facilities, staffed with scientists with a deep knowledge base in biomedicine, but interactions with researchers at Yale and other local universities were limited. None of these companies established institutional relationships with local research institutes, relying instead on opportunistic specific interactions between their investigators and individual researchers at these institutes.

I.4. State and Industry Relations

- 10 Until 1996, the state of Connecticut provided no incentives for the development of the biotechnology industry³. Two biotechnology companies, including Genlogic, actually chose to leave the region during this period, complaining of a lack of support (space and finance).
- 11 At that time, too, there was no state-wide organization representing the biotechnology industry specifically, only the Connecticut Technology Council, an industry association that represents all of the high technology companies in Connecticut. However, in 1990, responding to public concern over the safety and ethical implications of biotechnology in general and animal research in particular, the local pharmaceutical companies in Connecticut had established a 501c (3) non-profit organization called CURE (Connecticut United for Research Excellence). CURE's mission was to educate the public on biotechnology, specifically on the use of animals in research. Initially, CURE was not intended to be a lobbying or a representative body for the industry.
- 12 Thus, examining the region in the period prior to 1993 and up to 1996, we find many of the resources that could have been the basis of a biotechnology cluster. Previous

studies highlight that the importance of a strong academic base and proximity to universities and research institutes is highly important to the biotechnology industry. (Zucker, Darby *et al.*, 1998 ; Cooke, 2001 ; Coriat, Orsi *et al.*, 2003). Other studies suggest that resources in the form of large research laboratory within pharmaceutical companies, interactions with commercial firms, and availability of labor force, which existed in the region, are also important factors in cluster creation, especially biotechnology (Orsenigo, 2001 ; Breznitz and Anderson, 2006). Yet by 1993 there were only five local biotechnology companies in Connecticut (compared to 129 in Massachusetts at the same point)⁴⁵.

II. – Why and How Did the Transition Occur ?

- 13 In the early 1990s, when biotechnology firms were growing steadily in the world, New Haven had missed the information technology (IT) boom and was very keen on seizing the biotechnology opportunity. This section reviews the investment in economic development made by different players in the region, which was lead by Yale University...

II.1. Choices and Changes – the Role of Yale University

- 14 By 1993 the university, which was a leading institution in life-sciences, was concerned that the lack of industry and industry collaborations will harm the ability of the university to attract and retain star scientists and bright students, thus, damage university research and reputation.

What was happening was the university was starting to become concerned that it would detract from our ability to compete, to attract the best and brightest students, the best and brightest faculty, et cetera, if we didn't do something about it... First and foremost it was all about enhancing our reputation as a university, and two things come from that. One is our ability to attract and retain the best and the brightest faculty and students, and the second is to diversify the regional economy. Those were probably the principal reasons, and we weren't against making money, but we weren't making a lot at the time. It really wasn't the principal motivator, it really was about our reputation
(Interview with Yale Director).

- 15 The city's crime rate made New Haven an unsafe place for Yale's students (Atlas, 1996). Yale's chose to fight against local crime by working with the city of New Haven to revitalize the downtown area, and assist its employees to purchase homes in the city⁶. Specifically, a \$ 2 million project in 1993-1994 put streetlights on nearly every corner of the Yale campus, an emergency campus phone system was installed, and every entryway on campus relies on electronic entry. As a university within a city, Yale's efforts were viewed as urban regeneration.
- 16 Richard C. Levin was appointed as the twenty-second president of Yale in 1993. He took over the university at a time when concerns for recruitment of faculty, students, and the need to create a secure environment for students were of uppermost importance. This allowed Levin to implement a vast social, cultural, and economic development change in Yale. Coming into office in 1993, Levin in his first speech emphasized the importance of Yale's contribution to the local economy :

Our national capability in basic research was built by the far-sighted policy of public support for university-based science articulated during the Truman Administration and pursued consistently, though with varying intensity, ever since. Today, the scientific capability of American universities is the envy of the world. We neglect its support at our peril. As we seek to educate leaders and citizens for the world, as our discoveries spread enlightenment and material benefits far beyond our walls, we must remember that we have important responsibilities here at home. We contribute much to the cultural life of New Haven, to the health of its citizens and to the education of its children. But we must do more. Pragmatism alone compels this conclusion. If we are to continue to recruit students and faculty of the highest quality, New Haven must remain an attractive place in which to study, to live, and to work
(Levin, 1993).

- 17 The interviewees that participated in this study overwhelmingly agreed that the catalyst of the change in Yale's attitude toward research with potential practical applications was the arrival of Richard C. Levin in 1993. Levin, an economics professor, had a vision for Yale. He wanted Yale to be a « contributing institutional citizen » with a long-term commitment to the community (Levin, 2003). By referring to Yale as a « contributing citizen » Levin was referring to a broad range of activities at the university and not solely its role as an enhancer of economic development.
- 18 To pursue this vision, the university conducted an in-depth study of the activities already performed by Yale in the community and decided to invest in four areas : economic development, strengthening neighborhoods, revitalizing the downtown area, and improving the city image.
- 19 In order to support the focus on economic development, Yale rebuilt its technology transfer office, the office of Cooperative Research (OCR). The original Office of Cooperative Research was established in 1982, and dealt primarily with licensing and tracking patents. There was no real attempt to create or promote technology transfer from the academic to the industrial arenas, although a notable success before the rebuild was the compound licensed to Bristol-Myers-Squibb that became the highly successful drug Zerit® (Stavudine). Initially this license produced little or no income to Yale, but by 1998 it was generating royalty income of 30-40 million dollars annually.
- 20 In 1995, President Levin and Yale's provost at the time, Allison Richard, who in 2003 became the Vice-Chancellor of the University of Cambridge, persuaded Gregory Gardiner, a former Pfizer executive, to head the restructured Office of Cooperative Research. Gardiner, a former member of the Yale chemistry faculty, remembered the earlier lack of enthusiasm at Yale for research with practical applications, and was eager to help bring about change. Gardiner's expanded mission changed the function of the Office of Cooperative Research.

The duties of the OCR include oversight for patenting and licensing activities, university inventions, and contractual relationships between faculty and industry. OCR staff works with Yale researchers to identify inventions that may ultimately become commercial products and services useful to the public. OCR staff engages in industrial partnerships to license Yale inventions. An important goal for the Yale OCR is to identify new ideas, cultivate venture funding for them, and facilitate their development into companies that become part of the New Haven economy (Office of Cooperative Research Website, 2003).

- 21 Thus, the new Office of Cooperative Research would actively promote technology transfer, new firm formation spinning out from the university, and local economic development.
- 22 There were many obstacles facing Gardiner and his team. One of the biggest challenges was to communicate the new priorities and incentive structure to the Yale faculty.
- I was asked many times by junior faculty, « if I get involved with new ventures through the OCR, will I still get tenure ? » I told the committee [Educational Policy Committee of the Yale Corporation (the Yale trustees)] that we have to get Yale faculty to understand it is OK. At MIT, history says that this is OK but at Yale we need a change of culture (Greg Gardiner, Former Director of the OCR).
- 23 This quote highlights the difference between policy creation and policy diffusion. While Yale changed its policy its affects would not take place until the change become widespread. In order to achieve this goal of institutional cultural change, the OCR had discussions with departmental chairs and faculty to explain the institutional change and Yale's commitment to individual involvement in economic development. The Office of Cooperative Research representatives approached faculty who worked on applied research and had made important discoveries in the past. One of these faculty members recalls :
- The OCR people came to professors who had records in licensing or industry interaction and asked for ideas to patent and establish companies. They came to my lab, they knew I worked in XXX and XXX. One of the compounds went to « company name ». They also recruited the management for the company.
- 24 An examination of the disclosure process, the process by which a faculty member discloses his invention to the university, found that there was a need to change the process so as to prioritize the inventions that were most likely to succeed. The examination resulted in a major policy shift where OCR would seek out new inventions early, examine them quickly, and invest time and effort only in the strongest candidates. In addition, the upgrading of Office of Cooperative Research practices led to the identification and recovery of more than \$ 220,000 of unpaid royalties from several licenses. Also, recognizing that 80 % of patents from Yale were in the biomedical field, the OCR opened another office in the School of Medicine with four staff members (Office of Cooperative Research, 1998).
- 25 The Office of Cooperative Research's activities were characterized by active promotion of commercialization of research on a local level, not merely passive acceptance. For example, during 1996-1997, the OCR established direct contacts with venture capital firms, since lack of funding was an issue for many of the university spinouts. Their goal was not only to persuade venture capital firms of the relevance of university technology but also to convince them of the importance of creating new ventures in New Haven. Their hard work of seeking appropriate investors eventually paid off and in 1998, after two years of efforts, the first round of financing was concluded with \$ 20 million for five companies.
- We have all kinds of venture capital. One of the dirty little secrets is that although Boston thinks of itself as a major financial capital, we've got one that's even bigger. It's called Stamford Greenwich. When there was no state income tax, all the bankers used to live in Stamford Greenwich, not in New York City. So they all are still there, and that's where they have their finance companies' (Interview with Yale Administrator).

- 26 An equally important problem was the lack of appropriate infrastructure, such as laboratory space for new business ventures, as well as urban amenities to make New Haven attractive to mobile scientists and academics. In order to assist in the development, President Levin used Yale's ability to recruit top talent and in 1998 convinced Bruce Alexander, a prominent figure in urban regeneration to join Yale's office of New Haven and State affairs⁸. As explained by a Yale official :

And it became clear that there's no better person to kick out the economic development kind of mission that Yale would like to have than a guy like Bruce, so Rick « president Levin » convinced Bruce to take it on full time. It's one of those things where you sit around going, « it's nice that everyone wants to do this », but how many people are going to be able to tap a guy like Bruce Alexander to be their economic development guru ? The guy who redeveloped the Harbor place in Baltimore, the guy who did South Street Seaport in Manhattan. It makes us all look smart, but it's what a university like Yale can do.

- 27 The OCR, with the office of New Haven and State Affairs at Yale, led by Bruce Alexander, set out to build laboratory space close to Yale's scientists. Accordingly, the university attracted two developers, Winstanley Associates and Lyme Properties, LLC, both of which had experience in building labs. Winstanley bought the vacant headquarters of the telephone company on George Street, and Lyme took over the development and management of Science Park on north campus (where the university and the city had been trying unsuccessfully for years to build a science park). At the same time Yale invested in its properties in the downtown as part of making the rundown New Haven a safer and more enjoyable city. For example, in its Broadway street properties Yale created a mix of both local businesses and national chains – transforming the area into a vibrant shopping area and late-night gathering spot.
- 28 As a result of Yale's efforts to change its attitude to technology transfer, commercialization, and economic development, Yale created physical as well as cultural changes. While Yale did not set cultural change toward economic development as a direct goal, it became unavoidable. While the university invested in its technology transfer office and officers, in rebuilding the downtown area, and assisting in the development of laboratory space, and connections to industry, it demonstrated to faculty that the university is determined to support applied research and commercialization. This attitude change, as well as the arrival of faculty from universities that already had a tradition of working with applied research and commercialization influenced some hesitant faculties to venture into commercialization or even entrepreneurship.
- 29 Today the Office of Cooperative Research sees itself as a catalyst of local economic development, but hopes that in the future its involvement will not be as important. The missions of the OCR today are to benefit the community by transferring academic inventions to the public, to enhance the reputation of Yale University and its faculty, and to contribute to local economic development, while in the past the office focused solely on patenting and licensing. It took six years (1993-1998) to implement the changes at Yale and at the Office of Cooperative Research specifically. In August 1999, Greg Gardiner retired and Jonathan Soderstrom was appointed his successor as director of the OCR. As a result of the efforts by Yale in general and the OCR in particular, twenty-one biotechnology companies have been established in the New Haven Metropolitan Area, and many more are in development, as described in Table 1.

- 30 Table 1 summarized the Office of Cooperative Research accomplishments from 1996 till 2000. During this time licensing revenues grow from \$ 5,007,485 in 1996 to \$ 46,121,239 in 2000, a growth of 821 %. New licenses grow from 28 in 1996 to 47 in 2000, a growth of 68 %. Number of patents issued grew from 13 to 143, a growth of 197 %. Today, Yale has sixty-one spinouts in total and thirty-nine biotechnology spinouts. It is important to note that the OCR does not only build local companies. From the 70 licensing agreements put in place by the OCR in 2003, only 10 were with local companies, the rest were licensed out of state and on an international level. However, while the OCR promotes the transfer of Yale's technology to industry in general, not only on a local level, Yale is strongly committed to the local economy.

Table 1 - OCR Activities 1996-2000 ⁹

Activity	1996	1997	1998	1999	2000
New Licenses	28	25	45	20	47
Total Number of Active Licenses	233	190	235	244	270
License Revenue	\$ 5,007,485	\$ 13,091,174	\$ 33,306,248	\$ 40,720,584	\$ 46,121,239
Total U.S. patent applications filed	48	48	83	97	143
U.S. patents issued	13	24	24	33	32
Start-up Companies formed (9)	3	1	6	3	6

Source : Office of Cooperative Research, 1999-2000 ¹⁰.

II.2. The role of the state, the city, and industry

- 31 Until 1996, the state of Connecticut provided no incentives for the development of the biotechnology industry¹¹. However, in 1998, based on the work of 125 business leaders from Connecticut, six industries were identified as key sectors for Connecticut's economic development, including biotechnology. Basing its efforts on Michael Porter's cluster methodology, the state launched an industry cluster initiative under the Department of Economic and Community Development. The first attempt to launch a cluster was the bioscience cluster.
- 32 There are two entities representing the state of Connecticut in this effort. The first is *Connecticut Innovation* (CI). Created by the legislature in 1989, Connecticut Innovation was charged with investing in local companies in order to enhance economic development. CI was originally funded by the state. But since 1995, CI has financed its equity investments solely through its own investment returns, not through taxpayer dollars. It became the state's leading investor in high technology. The mission of the organization is « Making equity investments in emerging Connecticut technology companies ; providing essential, non-financial support to entrepreneurs ; and conducting initiatives that address specific needs of Connecticut's technology sector » (Connecticut Innovations 2003). CI has several ways of investing. Although generally it is an active investor, participating in creating a company, writing the business plan, and helping to select the management team, CI sometimes joins in the bridge round or Series A of the financing process¹². Carolyn R. Kahn, PhD, a bioscientist by training, was

appointed to lead CI's investments in bioscience in 1998¹³. Two major sources of funds are available to the local biotechnology industry :

- *The Connecticut BioSeed Fund*. Similarly to German government investments in biotechnology, BioRegio program (Adelberger, 1999), this \$ 5 million fund, administered by CI, provides seed capital to address the initial financial needs of young Connecticut companies, sustaining them until they are able to attract a lead institutional biotech investor for a Series A round of financing.
 - *The Bioscience Facilities Fund*. This \$ 60 million fund is used to underwrite the development of incubator and lab space. The state legislature created the fund in 1998, with \$ 30 million of state monies, and charged CI with its management. CI contributed an additional \$ 10 million, using proceeds from its equity investments. Since then, the fund has committed more than \$ 20 million to finance more than 225,000 square feet of laboratory and related space (Connecticut Innovations 2003). This particular fund was unique... In the late 1990s most of the national and private investment in biotechnology did not provide funding for laboratory space. In many cases companies could enter incubators owned by local or national governments, but direct funding to build a laboratory was not available.
- 33 The second state initiative to promote the Bioscience Cluster is the Office of Bioscience. With the second cluster bill in 2001, the state of Connecticut allocated \$ 100,000 to establish the Office of Bioscience within the Department of Economic and Community Development. The office has three employees, one of which is also working part time at the industry association, CURE (see below). The Office of Bioscience was built to support start-up and existing companies in the region, to provide all the necessary information on conducting business in Connecticut, to bring new and existing out-of-state companies to the region, and to represent the life science cluster of Connecticut in national and international events (interview with one of the office's executives).
- 34 Similar to Massachusetts, California, and North Carolina, Connecticut also provides tax incentives for the biotechnology industry (Mass Biotechnology Council (MBC) and Boston Consulting Group (BCG), 2002). These include the 1996 Biotechnology Tax Incentive Package that provides exemptions from sales, use and property taxes, and a fifteen-year carry forward R&D tax credit ; the 1999 Tax Credit Exchange in which eligible companies that cannot use their research and development tax credits can exchange them with the state for 65 % of their value ; and the Sales Tax Relief -50 % and 100 % exemptions are available on certain biotechnology industry materials, such as tools, fuels, equipment, and safety apparel.
- 35 Besides the state initiatives, the industry created institutions to promote biotechnology. The main example is Connecticut United for Research Excellence (CURE), the industry association. CURE's main activities are (a) lobbying for the interests of the bio-pharmaceutical industry, specifically seeking to preserve tax incentives for the industry at a time when the state is running a large budget deficit, and also working to develop a qualified labour force for the industry by creating certificate programs in local colleges ; (b) educating the public in general, and children in particular, on the science of biotechnology through the BIOBUS program, hoping to stimulate interest in studying and working in life sciences ; and (c) acting as a conduit for information needed by the industry (how to manage a laboratory, how to build an animal lab, etc.). Under CURE's auspices, local firms' top management, such as their Chief Executive Officers, Chief Financial Officers, and Public Affairs and Human

Resource executives meet quarterly to share information on similar problems and solutions.

- 36 Not all state assistance is directed towards R&D. Perhaps most important are safety and infrastructure concerns. The City of New Haven contributed to the development of the biotechnology industry by providing it with basic infrastructure and addressing safety concerns, such as streetlights and building sidewalks, especially in the area adjacent to Science Park on 300 George Street, located in one of the neighbourhoods with the highest crime rates in the city.

The city administration is doing more than I expected. They support business. This area here was not a very good part of town, they renovated the area, put streetlights. We did not have a single incident of assault. The city government should take credit for that. The police force is very responsive (Interview with biotechnology executive).

- 37 In summary, although Connecticut and the city of New Haven's support for university-industry relationships in general and for the biotechnology industry in particular started only in the late 1990s, the region has a wide net of support for economic development. This support by the federal and state government and industry is evident in tax incentives, new venture funding, lobbying groups, and policy-related logistical assistance. Much of this support is similar to national and regional efforts in Europe and other US states (Adelberger, 1999 ; Mass Biotechnology Cluster (MBC) and Boston Consulting Group (BCG), 2002 ; Breznitz and Anderson, 2006).

III. — The Impact of Yale's Economic Development Initiative

- 38 Today, the New Haven biotechnology cluster has forty-nine companies, including twenty-four companies, or 49 %, which were created with technology, ideas, or founders from Yale and with the help of the OCR. A total of twenty Yale spinouts were established in New Haven after 1993, the same year Yale started to implement its changes. The majority of the biotechnology companies in this area work in the human therapeutic sector (See figure 2). This could be directly related to Yale's strength in life sciences and to the fact that 49 % of the New Haven cluster is based on Yale University spinouts. This includes companies working in more than one sector. The results, below, are based on the self-definition of fifteen companies interviewed within the cluster. The cluster employs directly 16,686 people. Most of the firms are small- to medium-sized, with less than 50 employees.

Figure 2 - The biotechnology cluster in the New Haven metropolitan area by sector

Source : Author.

- 39 Yale's change toward technology transfer and commercialisation made an impact on the state of Connecticut as a whole. As noted in table 2, Connecticut R&D expenditures in bioscience are constantly growing, where the majority of growth can be seen in the biotechnology companies. This has a direct correlation with the growth in total number of biotechnology companies¹⁴. In 2003, expenditures by the pharmaceutical industry in Connecticut, which dominates the expenses of R&D in the state, accounted for more than 12 % of all R&D dollars spent by pharmaceutical companies nationwide (Connecticut United for Research Excellence (CURE), 2003). This represents extensive growth compared to the 6 % spent by pharmaceutical companies in Connecticut in 1995, when there were only six biotechnology companies in the region.

Table 2 - The bioscience cluster by R&D expenses in Connecticut

R&D expenses	Year End 2000	Year End 2001	Total Growth	% Growth
Biotechnology companies	226,154,159	277,210,873	51,056,714	23 %
Pharmaceutical companies	2,434,900,000	2,904,933,799	470,033,799	19 %
Academic institutes	391,231,208	429,893,436	38,662,228	10 %
Total R&D expenses	\$ 3,052,285,367	\$ 3,612,038,108	\$ 559,752,741	18 %

Source : Cure, 2003.

III.1. The Impact on the Local Pharmaceutical Companies

- 40 The strength of the local biotech industry has changed the way existing pharmaceutical firms interact with other players in the region. The local pharmaceutical companies have significantly changed their behaviour and funding patterns, and give more weight to the local intellectual base. There are constant connections between local pharmaceuticals and the local universities and research institutes, cultivated by Yale's OCR, CURE, and the Office of Bioscience. These connections include, but are not limited to, Yale and the University of Connecticut. Pfizer, for example, chose to utilize the local knowledge base by developing a direct relationship with Yale. Pfizer invested \$ 35 million in a 60,000 square-foot clinical trial facility in downtown New Haven between Park and Howe Streets, on land which is owned by the state of Connecticut. Additionally, Bayer initiated a scholar's program in 2003, which appoints a faculty member each year as a fellow and works closely with Bayer.

- 41 Today one can also find business relationships between local pharmaceutical firms and the local biotechnology industry. Neurogen Corporation, a biotechnology company, and Pfizer began a two-year research partnership in 1998 to work on GABA neurotransmitter receptor-based drug programs for the treatment of anxiety, sleep disorders, and cognition enhancement. Bayer and Curagen Corporation collaborate on obesity and diabetes co-development, pharmacogenomics, and toxicogenomics. R&D expenditures by the pharmaceutical industry in Connecticut have doubled since 1995, and in 2003 R&D expenditures accounted for more than 12 % of all R&D dollars spent by pharmaceutical companies nationwide (Connecticut United for Research Excellence (CURE), 2003) ¹⁵.

III.2. The Impact on Yale University

- 42 Examination of spinouts and patenting finds that Yale University spun out thirty-nine biotechnology companies, twenty-four locally, compared with only three in 1993, one locally. Moreover, in 2003, Yale University registered a total of 28 patents compared with two in 1993 ¹⁶. By 2000, 47 new licenses were issued, contributing to a royalty revenue of \$ 46.12 million (Office of Cooperative Research, 1999-2000).

III.2.1. The Impact on Yale Students and Faculty

- 43 Faculty members interviewed at the Yale medical school explained the numerous benefits in having local biotechnology industry :

Now, for example, we have a company that is occupying some space in the lab... It is good to have them here, because you have interactions with them and transfer of expertise (Interview with a faculty member at Yale).

- 44 Industry-university relationships allow scientific interactions, sponsorship of students, and access to expensive equipment not available at the university, and expose students to industrial practices. While working with companies has benefits for students and research, it has no bearing on faculty responsibilities, such as teaching, at the university. A faculty member who spins out a company, or provides consulting services, cannot reduce his or her teaching or administrative load.

No. [Founding a company] didn't have any effect on my university responsibilities. In fact the opposite occurred [the university benefited], when getting money from the company to go on retreats, or to buy a new microscope or something, the company would be able to participate in those activities and use that equipment (Interview with a faculty member at Yale).

- 45 Thus, the changes implemented at Yale did not change faculty responsibilities. However, the changes did contribute to university-industry relationships in the form of research grants and contracts, sponsorship of students, and access to industry equipment and experience.

III.2.2. Impact on the Office of Cooperative Research

- 46 Changes in the university also affected the Office of Cooperative Research. Today, the OCR employs eighteen people, each of whom has five to seven years of industry experience. The employee background at the Office of Cooperative Research had, and

continues to have, a crucial role in the cooperative relationships between local faculty and industry.

Yes. I do believe that [the people working at the OCR have the skill and knowledge to assess my technology]. I don't think there's any question. And I think that communication problem has gotten much, much better. From my biased point of view, I think it's enormously improved, and that they do a very good job at Yale (Interview with a faculty member at Yale).

- 47 Not only does the Office have the staff and expertise, it also is engaged with firm creation to an unprecedented level. The office is involved in developing product scenarios, financial projections, and business strategies with the scientists. In many cases, the Office is actively involved in building the company, looking for the right management and investors who will succeed in taking Yale's technology to the market.
- 48 The level of university-industry involvement within the Office of Cooperative Research is considered extreme. Even MIT, which is considered the top university in university-industry relationships, is not as involved in the creation of companies (Breznitz, O'Shea *et al.*, 2008).
- 49 As can be seen in figure four, twenty-four, or 62 % of Yale's thirty-nine biotechnology spinout companies chose to locate in the region. This suggests that Yale had a direct impact on the location choices made by spinouts. The wish to stay close to the university implies that companies positively view university research and resources.

Figure 3 - Yale University biotechnology spinouts, 1976-2004

Source : Author.

Conclusion

- 50 This paper describes the development of the biotechnology industry in Connecticut. The surge of new business formation was a result of efforts lead by Yale University. In

1993 Yale was facing several obstacles : though a strong research university in life-sciences situated in a close proximity to many pharmaceutical companies, the university had almost no industry collaborations or technology commercialization. The university had a very low rate of patents and licenses compared to the amount of research funding, and by 1993, compared to MIT that spun-out thirty companies, Yale spun-out only three. Moreover, the city of New Haven had become physically unsafe for Yale's students and faculty. All of these obstacles were perceived by university administrators as threatening its capability to draw students and faculty to the university, i.e. threatening its eminence. Thus, the university decided to rebuild its technology transfer office, with an aim to commercialize Yale's technology and contribute to local economic growth through the creation of companies and collaboration with the local industry. Furthermore, the university decided to invest in the city itself, i.e., investing in real-estate development of the university's old buildings as well as the city's downtown area, and assisting employees to purchase houses.

- 51 Yale was not the only agent of change in New Haven. The state of Connecticut opened a venture capital firm to invest in IT and life science companies that were willing to build their company in Connecticut. Moreover, unlike many other venture capital firms, Connecticut Innovation was providing funding for facilities and equipment. The city of New Haven assisted in the logistics of building sidewalks and street lights. The industry itself provided a meeting place and networking channel for both pharmaceutical and biotechnology companies. The total efforts of the different players resulted in the creation of a biotechnology cluster, and the building of university-industry collaborations.
- 52 Comparing the New Haven cluster development to some of the larger biotechnology clusters in the world, we find that the role Yale University played in this cluster is unique. In many of the biotechnology clusters such as Boston, Cambridge UK, and Silicon Valley, local universities are important and collaborate with industry (Breznitz and Anderson, 2006). However, they are viewed as suppliers of technology and labor force. MIT does not actively seek inventions and is not as much involved in the development of spinouts (Breznitz, O'Shea *et al.*, 2008). In the UK, both the University of Cambridge and Oxford University were the basis of the cluster's technological and humane resource sources. However, both universities were not actively involved in the creation of the cluster, nor was a national policy directed at the development of the cluster¹⁷ (Segal Quince Wicksteed, 1985 ; Segal Quince Wicksteed, 2000 ; Chiesa and Chiaroni, 2005 ; Solomon, 2005). On the other hand, in other countries in Europe and states in the USA, the biotechnology industry received similar regional level incentives to the ones in Connecticut.
- 53 In conclusion, this article's contribution is in the weight it gives the role of the university in cluster development. Unlike other industrial districts, the development of the biotechnology industry in New Haven was lead by Yale University.

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NOTES

1. This study is based on forty-five in-depth interviews with university administrators, academics, and senior management and researchers from biotechnology and local pharmaceutical companies, local trade association, government representatives, as well as city and state or national representatives.
2. One invention that was patented during this period was the profitable drug Zerit® (stavudine). This drug, which was licensed to Bristol-Myers-Squibb, is part of the AIDS drug combination treatment.
3. Compare to Massachusetts that recruited a specialist to deal directly with the biotechnology industry in 1991 after the recommendation from Governor William Weld's Commission on Growth and Competitiveness (Breznitz, 2000).
4. The five biotechnology companies that existed prior to 1993 in the New Haven area were: IBI (later bought by Eastman Kodak), Protein Sciences, Alexion Pharmaceuticals, Neurogen Corporation, and Curagen Corporation. Only one of these companies, Alexion Pharmaceuticals, had licensed its technology from Yale University.
5. The five do not include the two companies that had left previously.
6. To learn more about the four areas in which Yale made change, see President Levin speech on page 7.
7. Stamford and Greenwich are two towns in Fairfield County, Connecticut on the border with New York. In the 1980s many corporations including financiers moved from New York both to lower their tax bills and to be closer to the homes of their top executives, who chose to build their houses outside NYC. Thus, Connecticut has a large concentration of venture capitalists living in the New Haven Metropolitan area (which includes New Haven and Fairfield counties).
8. Yale's ability to recruit top talent is demonstrated in the recruitment of both Greg Gardiner from Pfizer and Bruce Alexander. This also confirms the notion that Yale had a choice of who to recruit and when to recruit them.
9. In total, not just in the New Haven Metropolitan Area, and not just biotechnology.

10. The information provided in this table reflects all fields of technology and not just biotechnology.
 11. While Connecticut did not provide any incentives for the biotechnology industry, Massachusetts recruited a specialist to work directly with the biotechnology industry in 1991 after the recommendation from Governor William Weld's Commission on Growth and Competitiveness Breznitz, Shiri M. (2000). *The Geography of Industrial Districts: Why Does the Biotechnology Industry in Massachusetts Cluster in Cambridge?* Master's Thesis, University of Massachusetts, Lowell. , Breznitz, Shiri M. and William Anderson. (2006). Boston Metropolitan Area Biotechnology Cluster. *Canadian Journal of Regional Science*. 28(2), 249-264.
 12. A bridge loan is a short-term loan that is used until a person or company can arrange more comprehensive long-term financing. The need for a bridge loan arises when a company runs out of cash before it can obtain more capital investment through long-term debt or equity. Series A preferred stock is the first round of stock offered during the seed or early stage round by a portfolio company to the venture capitalist. Series A preferred stock is convertible into common stock in certain cases such as an IPO or the sale of the company. Later rounds of preferred stock in a private company are called Series B, Series C and so on.
 13. CI invests in many industrial sectors that show potential for Connecticut economy. These include bioscience, information technology, energy and environmental systems, photonics, and others.
 14. As an example, we can see that the number of Yale's spinouts in the cluster grew by 50 % from 2000 to 2004.
 15. Compared to 6 % of all R&D expenditures in 1995.
 16. Yale and MIT in the same fields in 2000, Yale had 29 (the same as its total patents) compared to 58 at MIT (in the specific fields): a difference of 50 %.
 17. National policies in the UK such as the BIO-WISE were created in the late 1990s.
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ABSTRACTS

This paper analyzes the development of the biotechnology industry in New Haven, Connecticut. In 1993 there were only five biotechnology companies in Connecticut. However, by 2004 the state was home to forty-nine biotechnology and pharmaceutical companies. What led to this increase ? Through extensive field work, this research makes clear that the most important influence on the development of this cluster was that of Yale University. There is little doubt that the dominant influence was the change in attitude and policies of Yale towards biotechnology-based industrial growth, which took place after 1993. As such, the case confirms that universities can have an important impact on local industrial and economic development.

Cet article analyse le développement de l'industrie de biotechnologie à New Haven, dans l'État du Connecticut aux États-Unis. Alors qu'en 1993, cet État comptait seulement cinq firmes de biotechnologies sur son territoire, en 2004 on en dénombrait 49. Quels sont les facteurs à l'origine de ce phénomène? À partir d'une étude de terrain, cette recherche montre le rôle déterminant joué par l'université de Yale dans le développement de ce cluster. Plus précisément, l'article montre que c'est un changement d'attitude et de politique de l'Université vis-à-vis du secteur industriel des biotechnologies à partir de 1993 qui explique la croissance de ce secteur

dans la région. L'article conclut sur l'importance du rôle que peuvent être amenées à jouer les universités dans le développement économique et industriel local.

INDEX

Mots-clés: biotechnologies, Cluster, développement industriel, université

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