

BIOTECHNOLOGY IN CATALONIA. INDUSTRY ANALYSIS

Núria Mas

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Núria Mas¹

Abstract

Biotechnology is considered one of the key engines to achieving long-term sustainable growth. Catalonia is the main player in the Spanish biotechnology market, boasting 35 percent of the Spanish biotech R&D and 24 percent of its firms. In this report, we analyze the state of the Catalan biotechnology sector, focusing on its competitive advantages and disadvantages relative to other European biotech clusters. Our findings indicate that, in Catalonia, the biotechnology sector has the potential to affect sectors that represent 10 percent of the Catalan GDP and that employ 9.3 percent of the Catalan workforce. However, Catalan biotech is still quite small in relation to the top European bioclusters and it is only slowly catching up in some of its strategic components. The main advantages of the Catalan biotechnology sector are, first, its research effort, which has been improving steadily and that, especially in industrial biotechnology, has allowed Catalonia to start closing the gap with Europe. Second, the attractiveness of Barcelona to draw key staff. The main challenge it faces is access to funding and the fact that the size of related industries in the area is smaller than their size in the top European biotech regions. Finally, 65 percent of the Catalan biotechnology firms are devoted to the health sector, while the performance of biotech research in the industrial sector has been particularly competitive.

Keywords: Biotechnology, clusters, sector, Catalonia.

¹ Professor, Economics, IESE

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“We used to think our future was in the stars. Now we know it is in our genes.”

James Watson

Even though the exact link between research, innovation and economic growth is still not fully understood, the evidence of the importance of technology for economic growth in the economic literature is overwhelming. The recognition that the future of many businesses relies on the development of sound technologies is gaining adepts. In this context, it is not surprising that the development of science related to the biotechnology sector is rapidly gaining priority in many political and industrial agendas as more and more countries are considering it a key engine to achieving long-term sustainable economic and job growth. In fact, it is already specifically mentioned as one of the key strategic areas of the Spanish *Plan Nacional de I+D+I 2008-1011*; the Lisbon Agenda¹ and the EU Sustainable Development Strategy.²

Catalonia is one of the key biotechnology regions in Spain. It counts for 35 percent of the Spanish R&D expenditure in biotechnology and it is home to 24 percent of the Spanish biotech firms.³ However, the number of studies analyzing the relevance of Catalan biotechnology is very scarce, due, in part, to the lack of data on the Catalan biotech sector – for instance, biotech firms are not separately classified as such in the Idescat Database. Against this background, the aim of this report is to analyze the state of biotechnology in Catalonia and to present it in the worldwide context in order to understand the potential sources of competitive advantage/disadvantage of the region. Understanding the competitive position of Catalan biotech and its potential future prospects is particularly relevant because biotechnology is considered as a strategic sector by the government.

NOTE: With the collaboration of Javier Botella.

¹ EU (2000), “Presidency Conclusions: Lisbon European Council 23 and 24 March,” DOC/00/8. European Commission, Brussels.

² European Commission COM (2001) 264 final: Communication from the Commission – a sustainable Europe for a better world: a European Union strategy for Sustainable Development (Commission’s proposal to the Gothenburg European Council).

³ Asebio, 2007.

1. What is Biotechnology?

The OECD defines biotechnology as «the application of science and technology to living organisms, as well as parts, products and models thereof, to alter living or non-living materials for the production of knowledge, goods and services». Hence, as its name indicates, biotechnology is not a sector but a technology and as such it can have potential applications to a wide variety of industries. A color code is often used to facilitate the identification of those fields of application. Depending on the industries in which it is applied, biotechnology can be classified in four groups. The healthcare sector (red biotech) makes the greatest use of biotechnology. Here its science is employed in treating, diagnosing and preventing disease. In addition, biotechnology is widely used in agriculture (green biotech) and in the production of agro-food in general. Biotechnology is also applied in industry (white biotech), in the production of biochemicals, biomaterials and biofuels. Finally, blue biotechnology is a term that has been used to describe the marine and aquatic applications of biotechnology, but its use is, so far, relatively rare.

Biotechnology is, first and foremost, a *science-based* business where the quality of science is a key determinant for the economic value of the enterprise. This leads to many of these biotech firms being *funded by scientists* most of whom are university professors and quite a few of them remain as faculty. In Catalonia, 56% of the pure biotech companies have been funded by scientists.⁴ Actually, biotech start-ups are typically spin-off companies based on innovative products or processes resulting from discoveries within academic research.

Biotechnology contributes about 2 percent of the EU gross value added. However, it is still an *emerging* industry consisting of a few, very large companies and many very *small* ones. The average number of workers in a Catalan biotech firm in 2007 was 17,⁵ while in Europe it was 24 and in the United States it was 90.⁶ The biotechnology industry started in the United States and from there it spread throughout the globe. However, the distance from other countries with respect to the United States is still very substantial. There is now clear evidence of a maturation of the United States biotech industry, with strong pipelines and robust revenue growth, while Canada and Europe are progressively catching up. In 2004, 78 percent of the biotech industry revenues came from the United States while only 14 percent of them were originated in Europe⁷ (see Figure 1).

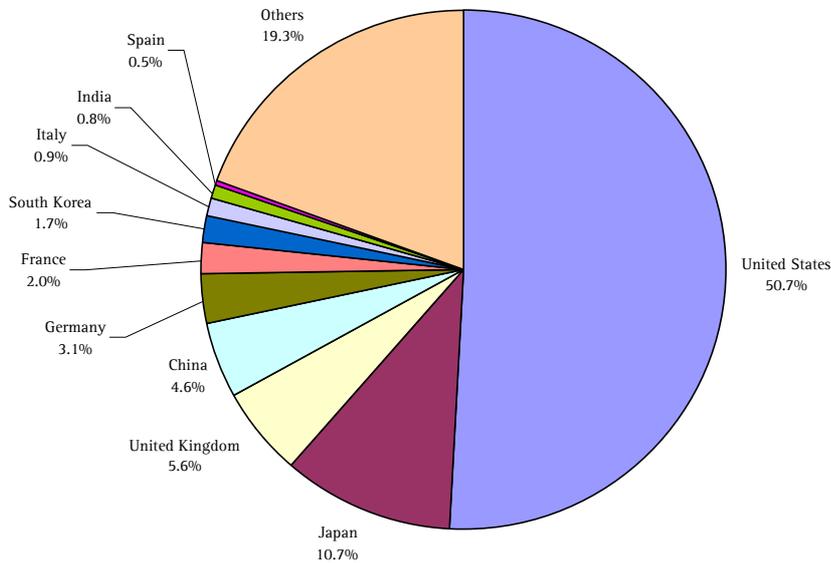
⁴ CataloniaBio Survey, 2005.

⁵ Genoma.

⁶ Ernst & Young 2007 global biotechnology report "Beyond Borders".

⁷ Ernst & Young 2005 global biotechnology report.

Figure 1
Biotechnology Market Share



Source: Datamonitor.

1.1. Industry History

A milestone marks the beginning of modern biotechnology: in 1953 Watson and Crick published a short article in “*Nature*” revealing the DNA structure. It took 20 years for Cohen and Boyer to perform the first successful recombinant DNA experiment, which allowed scientists to isolate specific genes. And it took yet another 7 years for biotechnology to establish itself as a possible business with the Genentech IPO. This marked the beginning of the first biotech wave. The commercial potential of the discovery and its successful IPO in 1980 created an enormous stimulus for other new entrants. Like Genentech, the new firms were typically founded by scientists from leading United States universities. The new entrants maintained extremely good links with universities, often licensing some of the basic technology from the labs of the cofounders and working closely with faculty and post-docs on research projects.

Table 1

Modern Biotechnology Timeline

↑	2006: Nobel Prize for the discovery of RNA interference Opening of the Barcelona Biomedical Research Park (PRBB)
	2004: <i>Catalan Bioregió is constituted</i>
	2003: <i>Completion of the sequencing of the human genome</i>
	2002: <i>CIDEM-PCB bioincubator</i>
	2001: <i>Opening of Barcelona's Scientific Park (PCB)</i> <i>Advancell is founded</i>
	2000: Center for Genomic Regulation is created <i>Oryzon Genomics is founded</i>
	1998: First biotech drug (neupogen) to achieve blockbuster status Discovery of the RNA interference
	1997: First cloned animal (Dolly)
	1994: Approval for a whole food produced through biotechnology
	1990: Human gene therapy is attempted successfully Human Genome Project begins
	1986: First biotech cancer drug is produced (Interferon) Genetically engineered plants (tobacco) are grown in field trials
	1984: Development of the PCR (polymerase chain reaction), that allows to amplify very small amounts of genetic material
	1980: First biotech IPO (Genentech) Bayh-Doyle Act: allows universities and faculty to stake patent claims on discoveries
	1978: Biogen, first European biotech founded
	1976: The technology of producing monoclonal antibodies is developed (Milstein & Kohler) Genentech Founded
	1953: Watson and Crick reveal the three-dimensional structure of DNA

1.2. Red Biotech (Biotechnology Applied to Health)

When it comes to biotechnology, red biotech is generally dominant. In the United States it represents 65 percent of all its biotech companies and 74 percent of all its employees. In Europe, the healthcare sector includes 55 percent of all the European biotech companies and it employs 65 percent of its workers.⁸ This is also the case in Catalonia, where more than two thirds of the firms contribute to the health, medical and diagnostics sectors. Out of those, 70 percent are dedicated to the development of new drugs and 25 percent to diagnosis.⁹

There is no doubt that biotechnology has tremendous potential in this sector where, for several years in a row, biotech companies have secured more approvals than their big pharma counterparts.¹⁰ A report to the European Commission¹¹ pointed out that, in 2006, biotechnology already contributed to 5 percent of the GVA of the European pharmaceutical market.

⁸ Europabio, 2006.

⁹ INE, "Encuesta sobre innovación tecnológica de las empresas" (Survey of companies' technological innovation), 2006.

¹⁰ Ernst & Young, 2007.

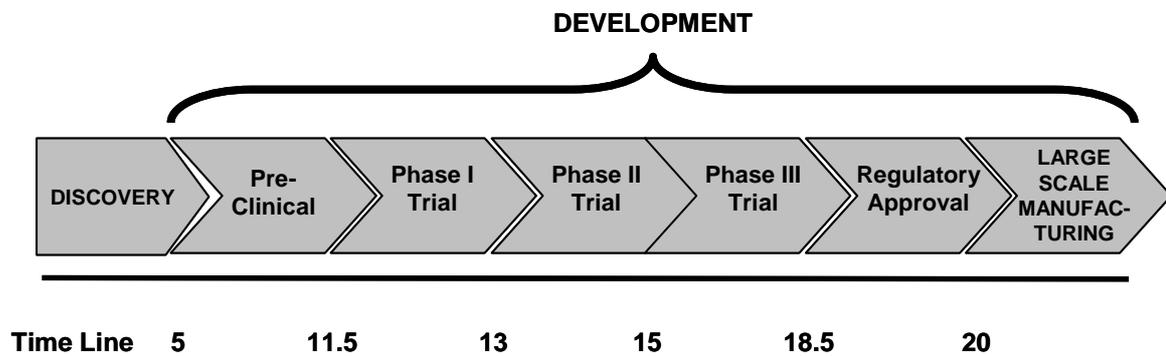
¹¹ See reference for European Commission (2007).

However, uncertainty still remains high. Statistics show that the probability of success of a new molecule that starts being developed (after several years in the discovery process) is only 1 percent. Hence, products that appear promising in the development phase might fail to reach later stages or be commercialized at all. Moreover, the process from the identification of a molecule to the marketing of a pharmaceutical based on it takes about 20 years.

The Figure 2 represents the value chain of red biotech for drug development and it includes the corresponding timeline for Catalonia:

Figure 2

Value Chain for Red Biotechnology



Technological uncertainty and a *long time lines* to reach the final market are the two main characteristics of red biotech and the ones that will most seriously condition its successful development.

The main attraction of red biotech lies in the fact that it may eventually lead to the discovery and development of a new product that might have been very hard or impossible to obtain with the classical pharmaceutical methods. If this new product is different enough from the existing ones and if it affects a sizeable amount of patients, this biopharma could become one of the key players in the pharmaceutical industry and make very substantial profits.

The current top biotechnology firms dedicated to the healthcare sector can be distinguished between product-oriented and platform-oriented firms. The first set of companies focuses on the discovery, development, production and commercialization of products. Amgen, Genentech or Genzyme are examples of this group of firms. The second group includes firms dedicated to the development and commercialization of new technologies and devices used in the discovery and development phases. Quest Diagnostics or Applera Corporation are examples of major platform-oriented red biotech firms.

Table 2

Ranking of Biopharma Companies (in revenue) in 2006

TOP 10 Blotech companies by 2006 revenues (USD Millions)							
Rank	Company	Country	Date of Incorporation	Revenues	R&D	Net income/ (loss)	Employees
1	Amgen	United States	1980	14,268	3,366	2,950	20,000
2	Genentech	United States	1976	9,284	1,773	2,113	10,533
3	Quest Diagnostics	United States	1969*	6,269	-	586	41,000
4	Genzyme	United States	1981	3,187	650	-17	9,000
5	UCB	Belgium	1928*	3,328	811	484	8,477
6	Gilead Sciences	United States	1987	3,026	384	-1,190	2,515
7	Serono	Switzerland	1906*	2,827	560	735	4,775
8	Biogen Idec	United States	1985	2,683	718	217	3,750
9	CSL Applena	Australia	1916*	2,079	117	256	7,575
10	Corporation	United States	1937*	1,949**	---	212	5,830

*Originally not biotech.

**Fiscal Year-End: June.

Source: Author's elaboration – Orbis. Hoovers.

1.3. White Biotech (Industry)

White biotechnology refers to the application of biotechnological methods and processes for the production of chemicals, materials and energy or the optimization of industrial processes. Europe is a key world player in white biotech, boasting, for instance, 75 percent of all the enzyme production in the world. The larger producers of modern white biotechnology goods and services are precisely enzyme producers, with top market players like the Danish firms Novozymes and Danisco's Genencor Int'l, which in 2007 had 44 and 21 percent of the world enzyme market share, respectively.¹²

A report to the European Commission (2007) already pointed out that industrial biotechnology contributed 5.85 percent of the European GVA. However, only 15 percent of the Catalan biotech firms are dedicated to industrial biotechnology.¹³

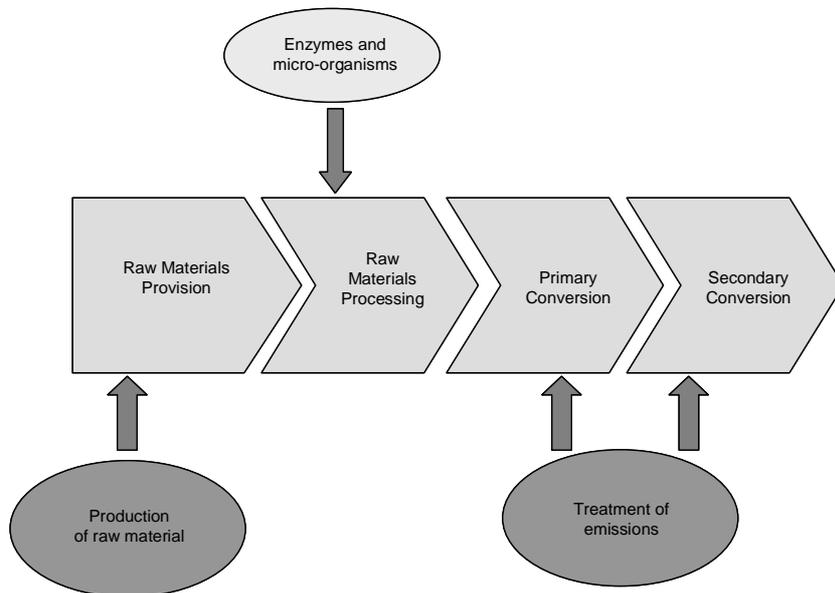
White biotechnology is used nowadays to manufacture a wide range of products and it can intervene at every stage of the manufacturing process as Figure 3 shows.

¹² Novozymes Annual Report 2007.

¹³ Genoma, 2007.

Figure 3

Value Chain for White Biotechnology



White biotechnology has a much shorter timeline than red; a new product or technological solution can reach the market in about 2 years. However, so far, the role of these firms has been more an auxiliary one, facilitating or accelerating an already existing industrial process and hence their potential of becoming a top player in the chemical or industrial market is more doubtful.

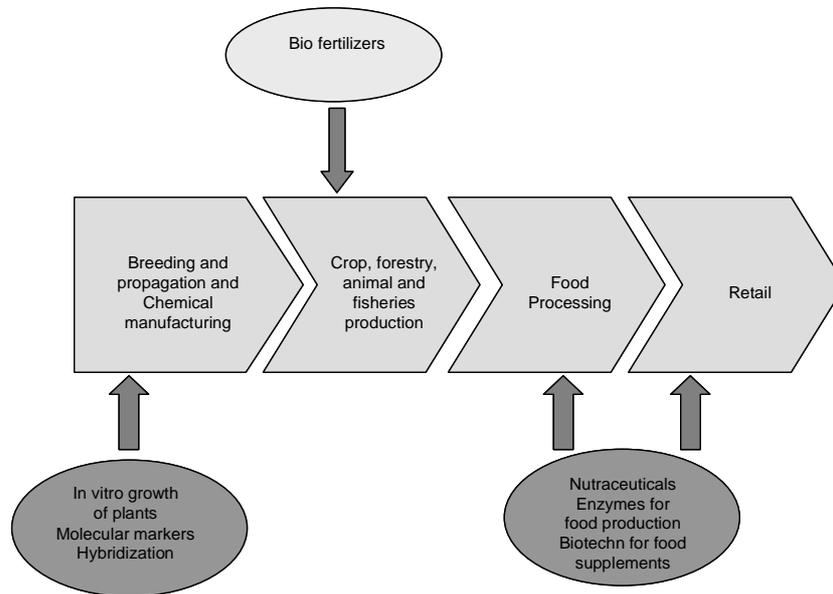
1.4. Green Biotech (Agrofood)

We can distinguish two main kinds of green biotech: first, these technologies devoted directly to agriculture. Some examples would be the *in vitro* technique that allows for the rapid growth of whole plants from minute parts of plants, the development of molecular markers that allow the selection of desirable traits in a plant such as its resistance to some plagues, and, also, genetic engineering of plants that lead to the production of new types of genetically modified crops. The second type of green biotech are technologies that are applied directly to the food industry, and they range from the development of *nutraceuticals* (new foods that claim to have health benefits) to new techniques that facilitate the inclusion of supplements to the food industry. Major companies, by 2007 revenues, operating in the green biotech market include Syngenta AG (€6,329m), Monsanto Company (€5,865m), BASF SE's Agricultural Products and Nutrition division (€4,989m), DuPont's Agriculture & Nutrition division (€4,658m), Bayer CropScience AG (€5,826m) and Dow AgroSciences LLC (€2,588m).¹⁴

¹⁴ Hoovers, 2007. Companies' annual reports.

Figure 4

Value Chain for Green Biotechnology



In 2006, 11 percent of the biotechnology companies in Europe were dedicated to green biotech, 5 percent in the United States, and 12 percent in Catalonia.

Even though biotechnology could potentially be applied in many stages of the food value chain, it is currently mainly applied in the sectors providing inputs to primary production (propagation of plants and animals, breeding, etc.). In Europe, biotechnology is used in the production of about 20 percent of the European agro-food sector output.¹⁵

2. Biotechnology in Catalonia

2.1. Activity

Catalonia is a key player in the Spanish biotechnology market. According to Asebio, in 2006, Catalonia was the Spanish region that created the most new biotech firms (30 percent of the total). Today, Catalonia accounts for 35 percent of the Spanish R&D expenditure in biotechnology and is home to 24 percent of Spanish biotech firms. Of the firms fully dedicated to biotechnology, Catalonia hosts 41 of the 221 that are located in the Spanish territory (see Figures 5.a and 5.b).

About 65 percent of the Catalan firms fully dedicated to biotechnology are devoted to health and diagnostic activities. This corresponds to the same share of biotechnology firms dedicated to the medical sector as the United States, but is slightly higher than the European 55 percent. Such a high concentration in red biotechnology is less surprising if we take into account that the fine chemical sector represents 2.3 percent of the Catalan GDP and that more than 70 percent of

¹⁵ European Commission (2007).

the sector in Spain is found in Catalonia. However, Catalonia also has a very strong chemical sector that produces 43 percent of the Spanish value added and only a very small proportion of the biotechnology is dedicated to white biotechnology, as *Figure 6* shows.

Figure 5.a

Location of the Spanish Firms Fully Dedicated to Biotechnology



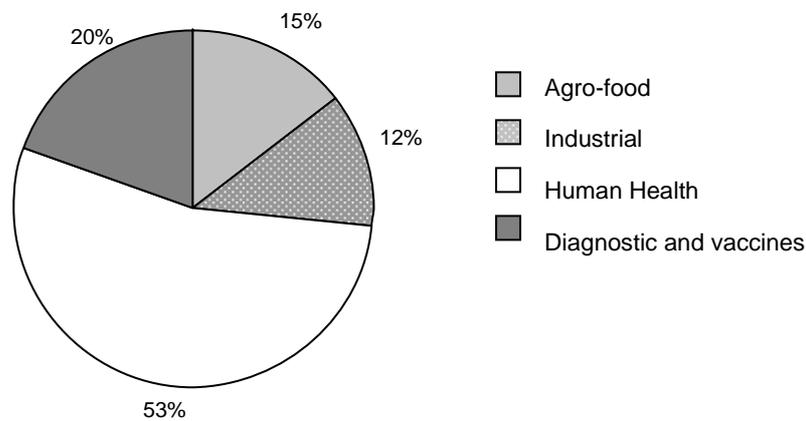
Figure 5.b

Location of the Spanish Firms Related to Biotechnology



Figure 6

Biotech Activity in Catalonia



Source: Author from Genoma data.

2.2. Size

Even though Catalonia is clearly a prominent player in the Spanish biotechnology market, its firms are quite small. In 2003 there were only 27 firms that had biotechnology as their core business, with an average of six workers. As *Figure 7* shows, they were also small and few compared to the size and number of firms in other bioclusters. However, both the number of firms and their size have experienced spectacular growth and, by 2007, there were already 41 firms fully dedicated to biotechnology, with an average of 17 workers (Genoma). In spite of this, Catalan biotechnology firm size is still below the American (90 workers) or the European (24 workers) average.¹⁶

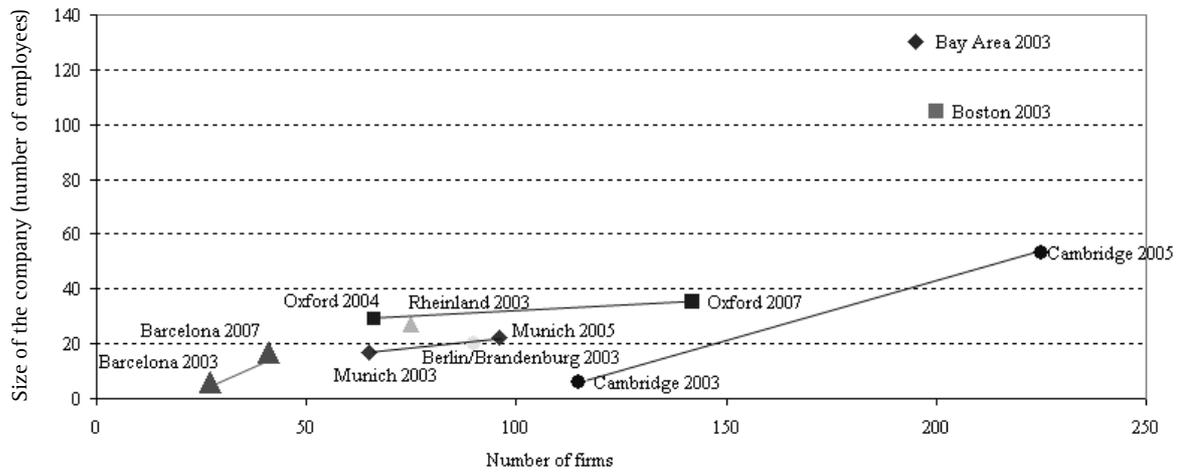
This fact is also true if we compare the Catalan bioregion with other European biotechnology clusters (*Figure 7*), and especially true if we compare the size and number of biotech firms in Catalonia with that of two top bioclusters in the United States, both of which are home to more than 200 firms.

The United States biotechnology sector is clearly much larger and more mature than the European one and, hence, the United States biotechnology firms have characteristics and needs that could be quite different from those of Catalan biotech. Given the important differences between the United States and Europe, from now on we will focus our analysis of the position of the Catalan biocluster in the European context, since it is a better benchmark for comparison for Catalonia.

¹⁶ Ernst & Young, 2007.

Figure 7

Comparisons of United States, European and Catalan Biotechnology Clusters

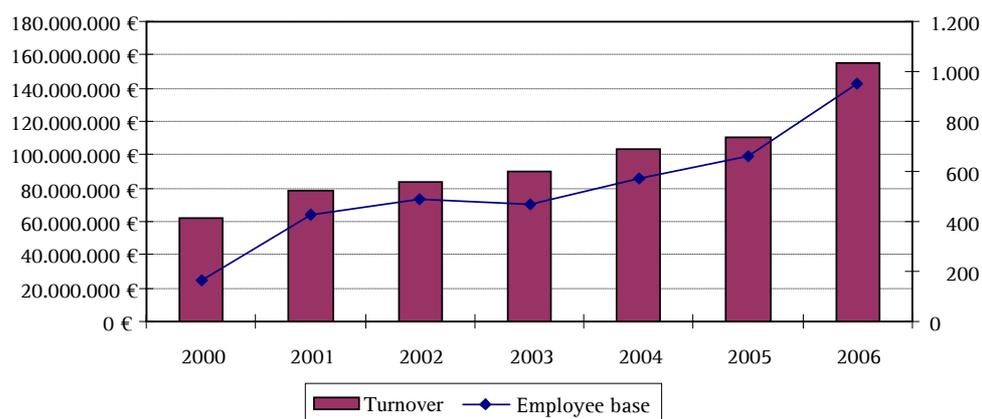


Source: Boston Consulting Group, 2003 and Genoma. Data 2005, NetBioClue. Oxford 2007, OBN Biocluster Report 2008, Oxfordshire Bioscience Cluster Report.

In the last few years, as the existing firms become more mature, the turnover of Catalan firms has also increased significantly, confirming that the sector is becoming more and more dynamic (*Figure 8*).

Figure 8

Evolution of Turnover and Employment of Catalan Biotechnology Companies'



Source: Author's elaboration. Data from Genoma España and SABI.

2.3. Quantifying the Potential Impact of Catalan Biotech in the Catalan Economy

In order to determine the potential impact of biotechnology on the Catalan economy, we follow the same methodology as the “Bio4EU Draft Final Analysis report”¹⁷ (henceforth, “Bio4”) from the European Commission. We consider all the economic sectors with biotechnology implications as those that are users of biotechnology techniques and those that are users of biotechnology-derived products. For each of these sectors (previously determined in the Bio4 report) we consider their contribution to Catalonia and the employment they generate.

Data used is from Idescat.¹⁸ Due to data availability, we used year 2006 for industrial and agriculture sectors and 2005 for services. Moreover, we have collected data from 2001 in order to see the time evolution of the biotechnological related sectors. The only exception here is the service sector “Technical testing and analysis” where 2002 was the closest data available.

The identification of the relevant sectors in which biotechnology can have an impact comes from Bio4 in the framework of the NACE¹⁹ classification where feasible. The Catalan economic sectors classification used in Catalonia (called CCAE²⁰) completely matches the NACE classification, so the equivalence by code number was easy.

Our results (detailed in Appendix A) indicate that the Catalan biotechnology sector has the potential to affect sectors that represent 10 percent of the Catalan GDP such as healthcare, pharma, the chemical industry, etc. These sectors currently employ 9.3 percent of the Catalan workforce (see Annex A for calculations).

2.4. Scientific Production and Quality

Basic scientific research has a strategic importance for the future survival of the Catalan biotechnology sector. In this respect, Spain has a clear advantage since, according to Genoma, it has been the fourth major publisher in biotechnology and microbiology in Europe after Germany, United Kingdom and France for the period 2000-2006. In 2007 Spain was the fifth contributor in the EU-15 in molecular biotechnology research just behind United Kingdom, Germany, France and Italy.

Given the crucial importance of research in this industry it is not surprising that, in 2003, 68 percent of the Catalan biotech firms had more than half of their workers dedicated to R&D.²¹

¹⁷ “Contributions of modern biotechnology to European policy objectives,” Draft Final – VERSION 31 January 2007 for the European Commission.

¹⁸ Idescat does not provide data for Veterinary activities, so we have used market studies. In other cases, where the disaggregation has been impossible, we have taken an aggregated sector, e.g., agriculture and fishing instead of breeding and seeds. This data was obtained from “L’aportació del sector sanitari a l’economia catalana” from Estudis Caixa Catalunya.

¹⁹ NACE is the statistical classification of economic activities in the European Community. In the Reference report, version 1.1 of 2002 is used.

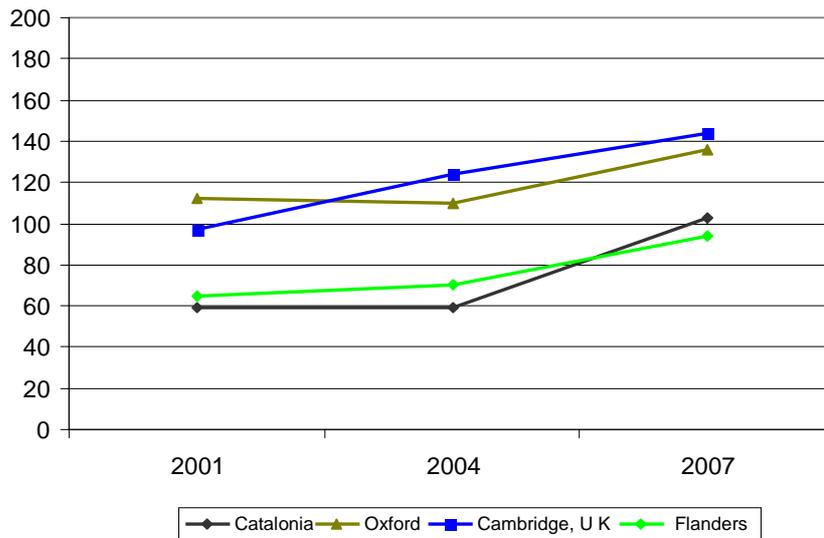
²⁰ In our report the CCAE-93 Rev.1 is used.

²¹ CataloniaBio survey, 2005.

This proportion is clearly higher than the European 47 percent average.²² *Figure 9* compares the number of scientific publications of several European bioclusters. Here we can see that Catalonia started from a very low position, but in the last three years it has been able to significantly reduce the gap with respect to the other European bioclusters. However, the impact of the Catalan publications is still low (*Figure 10*) even though it has also been improving.

Figure 9

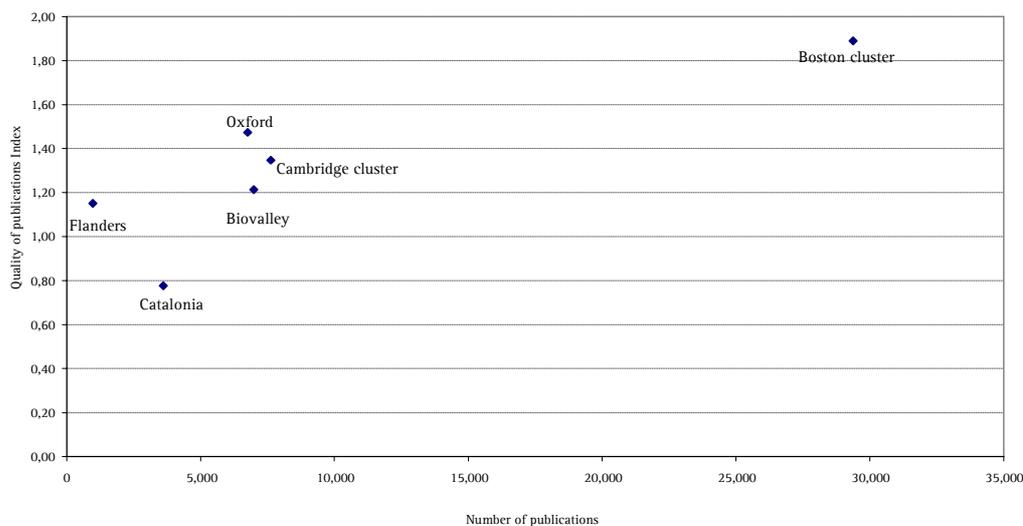
Number of Biotechnology Publications. Catalonia vs. other European bioUnited States



Source: Author Using ISI – Thomson web of knowledge data.

Figure 10

Quality vs. Quantity Publications in Biotechnology

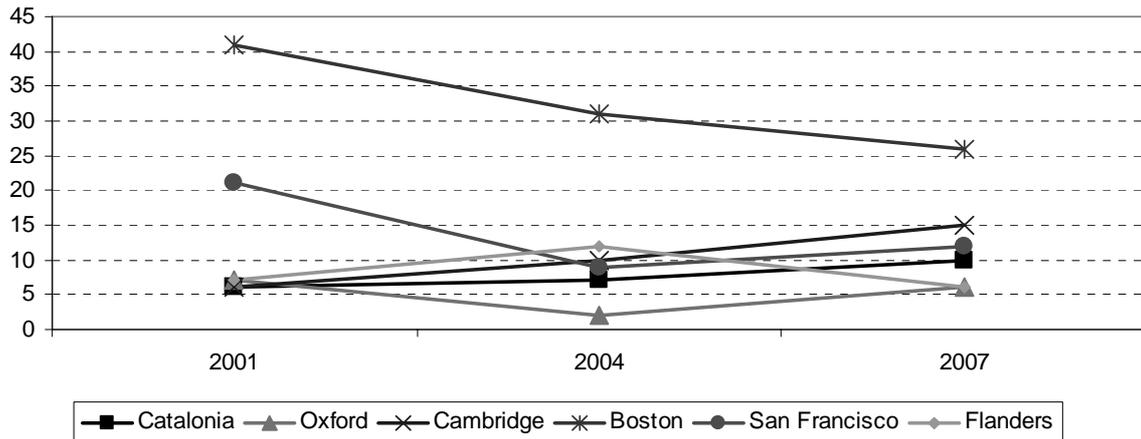


²² Critical I, 2006.

As we have already mentioned, the chemicals sector is quite strong in Catalonia; Catalan chemical companies produce 43 percent of the total Spanish value added. However, its importance is not mapped into the weight of the white biotechnology, which represents only about 12 percent of the whole Catalan biotech.

Figure 11

Number of Biochemistry Publications



Source: Author, Using ISI – Thomson web of knowledge data.

Figure 11 shows the evolution of Catalan publications in biochemistry. In this sector, the improvement with respect to other European bioclusters had already started in 2001, and now Catalonia’s scientific production in biochemistry is already above that of the Oxford and Flanders biotechnology clusters. Unfortunately, the ISI data does not allow us to weight the importance of the number of publications by their impact, as we have done in Figure 10.

However, these results are clouded by the *patent* data. On this front, both Catalonia and Spain lie way behind other biotechnology clusters. According to Genoma, Spain is at the bottom of the European ranking for patent acceptances (number 11th in the U-15) and only number 9th in the number of patent applications. In 2007, 30 Catalan Companies registered 54 patents either through the OEPM (Spanish patents agency), the EPO (European), the USPTO (in the United States) or, in most cases, the PCT (international patents). The total number of registered patents in Spain was 137 (Asebio). On the positive side, this represents a significant improvement in the last four years, given that the number of biotechnology patent applications in 2003 was only 66.²³

2.5. Product pipeline

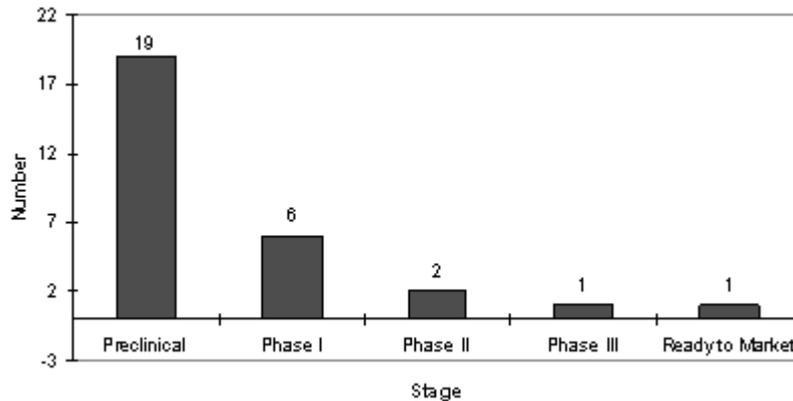
In 2007, 64 new products developed by Spanish companies were launched onto the market. Of those, ten were launched by Catalan companies (Appendix B, Table B.1.). Catalonia currently

²³ Eurostat, Patent statistics.

has 29 products in different stages of the development pipeline (*Figure 12*). As expected, the pipeline has the textbook funnel shape, continuously declining as we move up to later phases.

Figure 12

Catalan Human Health Medicine Pipeline Stage Distribution



Source: Author, based on Asebio's Spanish Red Biotechnology Pipeline. March 2008.

Table 3 compares the stage of the Catalan and Spanish biotechnology pipeline with that of other European areas. Due to data restrictions, Data for *Table 2* comes from two different sources: the data for Spain and Catalonia is from Asebio while data for the rest of Europe comes from Ernst & Young 2008 Report. This could explain the fact that the numbers for Spain look high compared to those for the rest of Europe; even more so if we take into account that, in their report, Spain was ranked number 10 out of 16 European countries. Given these discrepancies, we will focus our analysis not on the absolute numbers, but on the pipeline structure. It is interesting to notice that the United Kingdom, which has two very mature biotechnology clusters (Cambridge and Oxford) has only 39 percent of its products in the preclinical stage, while this number jumps up to 65 percent for Catalonia but only 45 percent for Spain as a whole. Products in phase III, on the other hand, represent 10 percent of the United Kingdom pipeline, while they are only 8 and 7 percent for Spain and Catalonia, respectively.

In terms of the nature of compounds being pursued, the Catalan pipeline is more diversified across the different therapeutic areas than the Spanish one, which is mostly focused in oncology (see *Figure 13*). This last one is more in sync with the observed European tendencies, where the top three therapeutic areas are oncology (28%), neurology (15%) and infectious diseases (13%).²⁴

²⁴ Ernst & Young (2008).

Table 3

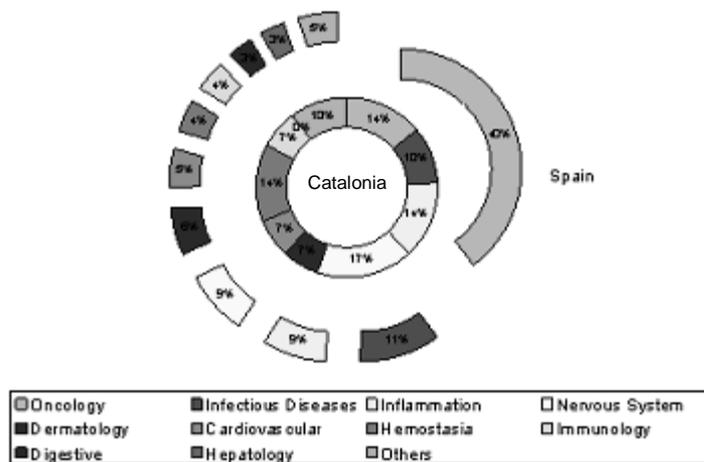
Red Biotech Pipeline in Europe, 2007

	Preclinical	Phase I	Phase II	Phase III	Total
United Kingdom	140	66	119	36	361
Germany	133	39	73	17	262
Denmark	65	46	60	17	188
Belgium	19	12	9	3	43
Netherlands	23	11	13	4	51
Spain	134	74	62	24	294
Catalonia	19	6	2	2	29

Source: Ernst & Young Global biotechnology report 2008. * Data for Spain and Catalonia is from Asebio.

Figure 13

Distribution of the Spanish and Catalan Red Biotechnology Pipeline (2008)



2.6. Funding

Since biotechnology is still an emerging sector in Spain, and in most of the other countries, public funding plays a very important role. In 2004, in Spain, 70 percent of all R&D expenditures in biotechnology were publicly funded. This was, for instance, slightly below the 75 percent public share of Norway.

In 2007, 80 percent of public funding was devoted to R&D in Spain (Asebio 2007). *Table 4* shows the evolution of R&D spending in biotechnology for Catalonia and Spain. In the period 2000-2006 this grew by 450 and 400 percent respectively. In 2006, 374 million Euros came from public funding (88 percent of the whole Spanish R&D investment).

Table 4

R&D Investment in Biotechnology (in million €)

	2000	2001	2002	2003	2004	2005	2006
Catalonia	5.82	7.98	11.57	16.35	25.12	28.07	32.08
Spain	85.44	117.88	167.96	221.83	271.18	322.75	422.00

Source: Genoma.

As is the case in many emerging sectors, biotechnology firms have to find new forms of funding. Venture capital has been of key importance, for instance in the development of the biotechnology industry in the United States which, in 2007, still boasted 72 percent of all the venture capital investments worldwide. However, the importance of venture capital in Spain is growing steadily. In 2007, Suan Biotech was constituted and in 2008 YSIOS just closed the largest Spanish venture capital fund completely dedicated to biotechnology.

Table 5 provides data on venture capital investment for several countries. The United States is clearly far ahead, but within Europe, Spain is gaining momentum and actually, venture capital investment for the period 2000-2006 grew a 205 percent. Moreover, in 2007, 17 Catalan biotechnology companies participated in financial operations considered by Asebio to be among the most important in the Spanish biotechnology sector in 2007. CDTI's Neotec participated in five of those operations and another set of investors participated in nine capital increases that brought the biotechnology firms an overall 14.9 m€ investment (*Table 5*). Also, eight Catalan biotechnology companies established a total of 24 partnerships 26% of which were established with non Spanish players (Asebio).

Table 5

Evolution of Venture Capital Investment

	United States	United Kingdom	Germany	Denmark	Belgium	Netherlands	Spain
2000	3,428	261.1	431.6	88.6	73.6	11.9	4.9
2003	1,948	250.6	171.3	42.1	26.1	17.5	3.6
2006	3,823	238	213	144	118	29	14.9

Source: Biocentury (2000 and 2003) and Ernst&Young (2006)/ own elaboration.

3. Competitive Strengths and Weaknesses

After briefly presenting the main characteristics of the Catalan biotechnology industry in the previous section, our purpose here is to evaluate the competitive position of Catalonia in six aspects that play a crucial role for the development of a biocluster and that were first pointed out by the Lord Sainsbury's Report on biotechnology (1999).

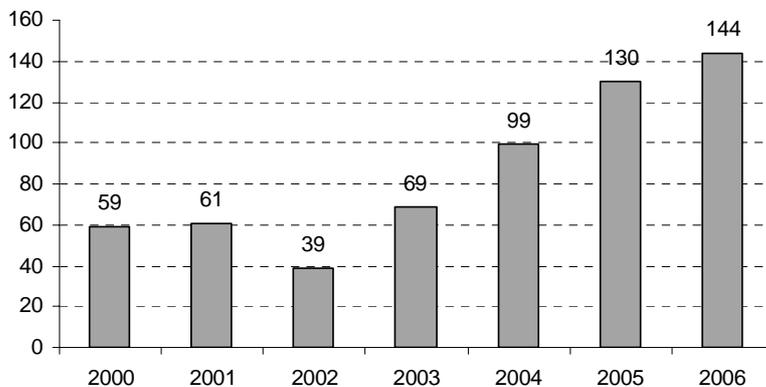
3.1. Strong Science Base

Leading edge science and a critical mass of research activity provide the lifeblood of biotech clusters. In this aspect, as we have seen in the previous chapter, Catalonia is still behind the research production of the top European bioclusters but is quickly catching up, especially regarding white biotechnology. Spanish research publications in biotechnology grew 27.3 percent from 2000-2006, while the average growth for the EU-15 was 4 percent.²⁵

The distance from Europe regarding patents is more important but it is also diminishing. *Figure 14* shows the progress in the number of biotechnology patents obtained in Spain.

Figure 14

Evolution of Spanish Biotechnology Patents



Source: Asebio/author.

Finally, Catalonia is home to an extensive network of public and private research institutes. The Catalan Science and Research Network includes 12 universities, 9 research centers, 6 research hospitals, 6 Science parks and numerous R&D departments of private firms.

3.2. Entrepreneurial culture

Entrepreneurship is often considered an important factor in explaining the differences in the rate of technical progress between countries. Its role is of particular importance for the development and growth of biotechnology since it is still not a mature industry in Catalonia (or in Europe in general). Moreover, a strong entrepreneurial culture will help ease the transition from scientific research to a final commercial product. Entrepreneurship will also offer opportunities to young scientists, providing them with a platform to take their basic research to the next level.

²⁵ Genoma.

However, measuring the entrepreneurship culture of a country or region is complex since there are many determinants of this practice such as national culture, legal environment, public sector size, etc. Many institutions attempt to measure it by conducting surveys of the population or of CEOs. Here we present the results of two of these surveys, which are the most commonly cited in business. The Global Entrepreneurship Monitor (GEM), for instance, assigned Catalonia an entrepreneurship index of 8.57% in 2006, above the averages of Spain (7.27%); the United Kingdom (5.77%) and Germany (4.21%). On the other hand, the Department of Economic Development of Dubai (DED) conducted an Executive Opinion Survey for about 200 Chief Executive Officers (CEOs) of major Dubai-based organizations in 2005, following the structure of the World Competitiveness report of IMD and including countries and sub-national regions. The next table shows the results of that survey for a selected number of countries, in three main variables related to entrepreneurship.

Table 6

Entrepreneurship Index

	Entrepreneurship	Ease of doing business	Firms Creation
Switzerland	6.11	7.14	6.88
Belgium	5.97	5.30	5.17
France	5.29	4.88	4.7
Germany	4.97	4.64	4.97
Catalonia	4.91	5.56	5.20
Spain	4.91	5.48	5.18
United Kingdom	4.88	5.98	5.76
Scotland	4.26	6.05	5.16

Source: Dubai's competitiveness advantage study. Legend: Entrepreneurship (10 - widespread in a country; 0 - not widespread in a country). Ease of doing business (10 - is a competitive advantage in the country; 0 - is not a competitive advantage in the country). Creation of firms (10 - supported by legislation in the country; 0 - hindered by legislation in the country).

3.3. Growing Company Base and Large Related Firms

Biotechnology Company Base

Having a critical mass helps to attract other companies, suppliers, investors and skilled labor to the biocluster. Moreover, as we have already seen, biotechnology can contribute to very many different stages of the value chain of the pharmaceutical, chemical and food and beverage production process. Hence, having a large surrounding base of companies (pharmaceutical, chemical, food and beverages, etc.) that could generate strong demand for the first stages of a new biotech technology is also of great importance to be able to develop biotechnology as a business. Proximity to large companies in industries related to biotechnology can also contribute to providing management expertise and partnering opportunities.

Even though the number of companies in the Catalan biocluster is still small compared to other European clusters (*Figure 7*), it has been growing steadily. Between 2004 and 2007 it grew 51 percent, while in Spain the overall growth rate of biotechnology firms was 32 percent and,

in Munich and Cambridge it was 36 percent. The turnover and number of employees of these companies have also been gradually increasing (*Figure 8*).

Large Related Industries

Apart from the number of pure biotechnology firms, one should also consider the importance of the existing base of industries that could generate demand for the different biotechnologies at several stages of their production process. In this respect, Catalonia accounts for roughly 23, 40 and 70 percent of Spain's total food, chemical and fine pharmaceutical chemical production, respectively. Because 65 percent of the Catalan biotechnology firms concentrate on red biotech, the pharmaceutical sector is one of the axes of the Catalan biocluster. Catalonia hosts 163 of the 377 pharmaceutical companies in Spain (Farmaindustria) and 66 percent of the Spanish fine chemical companies (Cidem).

Both the local and international pharmaceutical companies based in Barcelona account for 56% of the R&D expenditure in the Spanish pharmaceutical sector, but we should note that the Spanish R&D expenditure level (approximately 4.2% of turnover) is below the EU average of 15 percent (SPRI). This difference can be attributed to the facts that: a) it is a common practice for the multinationals to centralize the R&D at their corporate headquarters while conducting production activities abroad, and b) the limited size of Spanish pharmaceuticals in comparison to larger multinational leaders that play very important roles in other European reference bioclusters. For instance, Biovalley counts on the presence of Novartis and Roche amongst others.

Catalonia also hosts 38 percent of the Spanish medical device companies, among which we find manufacturers (with their own product or not), distributors, marketers and specialized services companies, segmented in a wide range of specialties (SPRI).

3.4. Ability to Attract Key Staff

According to Asebio's 2007 Survey, the most relevant factors currently facilitating the proper development of the biotechnology industry in Spain are the worker's skills, the easy access to qualified staff and the improvement of cooperation with universities and Technology Centers.

In order to succeed and to become a mature sector, biotechnology companies have to be able to attract the best management and scientific staff, competing with other countries and companies. Moreover, abundant and qualified research is a necessary condition not only to advance in cutting-edge science but also to attract and sustain investments by public and private entities. Clusters can facilitate this aspect by providing a scientific environment and offering a wide range of career opportunities in the field. Quality of life, being in a vibrant international city and remuneration are also keys to attracting strategic staff. According to the European Cities Monitor survey, Barcelona was the European city with the best quality of life for workers in 2006 and it has held this position for the last seven years.

On the other hand, the average remuneration in 2006 for researchers in Spain, €38,873, PPP adjusted, was slightly below the EU 25 average of €40,126 (PPP adjusted) and far lower than the United Kingdom average (€52,776, PPP adjusted) and Germany (€53,358, PPP adjusted).

Finally, in order to attract key management, the size of related firms such as pharmaceutical or chemical is also important because some of the biotechnology managers could come from the

related industries, as has been the case in the United States and the United Kingdom. In this aspect, the size of Catalan firms is generally smaller than that of their European counterparts.

3.5. Availability of Funding

As is the case in many developing industries, access to funding is essential for the development and establishment of biotechnology as a business. The funding challenge becomes especially important in the case of biopharma, given its two key characteristics: a lot of uncertainty and long-term investment.

Spain ranked only 43 in the 2007 Capital Access Index,²⁶ which ranks countries around the world in terms of the financial infrastructures that support entrepreneurial activity by providing access to capital. The United Kingdom ranked 2nd and Germany 17th.

Public funding for R&D projects plays a very important role (see Section 2.6 of this document). In Spain, it has mostly facilitated the development and growth of basic research and also in the creation of new infrastructures (*Parques Tecnológicos*). Moreover, in Spain there are public entities like the Center for the Development of Industrial Technology (CDTI), which has the objective of facilitating the creation of new technological firms, such as biotechnology ones. CDTI has two different tools to achieve this goal. First, to address the capital needs of recently created technological firms, it provides the NEOTEC program, which facilitates access to a maximum of €600,000 of seed capital. Second, through the NEOTEC CONSOLIDACION Program, to facilitate access to capital for biotech firms that are in the consolidation process. The maximum amount available is €1 million for firms younger than six years old.

Informal individual investors or business angels also intervene in the starting process of a firm. Business angel networks bring together angels and increase the efficiency and likelihood of matching angels and suitable entrepreneurs. In 2006, of a total of 211 networks identified in Europe by the EBAN (European Business Angel Network), Spain had 21, of which 8 were in Catalonia; by comparison, France had 35, Germany 41 and the United Kingdom 34. In 2004, Spain hosted 291 individual business angels, well below the 829 of Germany or 8,240 of the United Kingdom.

In 2005, BCN Ventures, a public-private fund, was constituted with the objective of investing in Spanish biotechnology firms.

As we have already pointed out (Table 5), there is still a big distance between Europe and the United States regarding the role of Venture Capital in general and in biotechnology in particular, with the United States receiving 72 percent of all the worldwide investments. However, access to venture capital is quickly improving for Catalan firms; for instance, two major companies were recently constituted: Suan Biotech (€30 million) and YSIOS (€70 million).

Another available option for the biotech firms that has not been used yet, is their possibility of accessing the Spanish Alternative Stock Market (MAB), which was constituted in 2005 with the objective of facilitating access to capital. Initially this was only to Venture Capital and SICAVs,²⁷ but since 2007 also to smaller firms. However, so far, even though several of the

²⁶ Milken Institute Capital access Index 2007.

²⁷ SICAV “*société d’investissement à capital variable*” - investment company with variable capital.

biotechnology firms we have talked to have shown interest in the MAB, none of them has used it yet. When asked why, they have mostly mentioned the current economic cycle.

Hence, it seems that in Catalonia access to initial capital, at least for the first three years and for the most basic research stages, is quite readily available. However, finding investors in the next steps of the value chain is proving to be more of a challenge. After several interviews with experts in the sector, we believe that there are two main reasons for this. One is that in Spain, and in Catalonia in particular, the potential investor base is not yet used to investing in such long risky projects. They are more used to thinking about *traditional* investments where the investment is based on a final product. In biotechnology, most of the investment should be thought of as an investment in expectations. The second reason is that access to international capital is not easy, especially at the beginning of the process. In this aspect there are already two alternative stock markets for smaller firms in Europe: AIM in the United Kingdom and Alternext in France. Considering participation in the MAB has pros and cons, therefore: on the one hand it is easier for smaller Spanish firms to be in the Spanish MAB than in the other foreign ones. However, on the other hand, the two existing markets already have an investor base used to providing capital to this type of projects. Plus, it might facilitate access of the firm to international investors.

According to Asebio's 2007 Survey, access to finance is still one of the major causes of concern for the biotechnology professionals concerning the proper development of the sector. This is particularly true for those firms that have already been in existence for several years. For them, access to public funds to start a business is no longer available and they are now facing the possible need of substantial financial injections in order for them to be able to continue to the next phase. In fact, in its Critical I report, Europabio already warned European biotech firms about the "*finance precipice*" they were facing after 7-10 years of existence. This situation might be particularly challenging in the current "credit crunch" economic environment.

3.6. Premises and Infrastructures

General infrastructure resources give us an ambiguous result about the situation of Catalonia in comparison to other European regions:

Catalonia is well provided for in highway infrastructures, with resources that are 20.2% above the 25 European richest regions average,²⁸ but Catalonia is 46% below in railway resources. In relation to Spain, Catalonia is below the average of infrastructure stock per inhabitant. The Catalan capital stock per inhabitant in roads, airports and harbors is only 88, 57, and 93 percent respectively of the Spanish average per inhabitant.²⁹ Catalonia is only above the Spanish average capital stock per inhabitant in railways (116 percent).

However, Barcelona is well placed regarding the availability of office space and technology parks, which play a very important role in biotechnology (Table 7). Taking into account the closest main cities to the European bioclusters, Barcelona ranked 2nd in office space in Europe just below London (the closest main city to Oxford and Cambridge).³⁰

²⁸ Measured by F index. See "Dotacions d'infraestructura l'opció de diferents models territorials."

²⁹ Institut Valencià d'Investigacions Econòmiques.

³⁰ European Cities Monitor, 2007. Cushman & Wakefield Healey & Baker.

The Network of Science and Technology Parks of Catalonia (*Xarxa de Parcs Científics i Tecnològics de Catalunya - XPCAT*) contains big spaces of production, transfer, diffusion and use of knowledge. It consists of centers and groups for university research, technological centers, large companies and their associate R&D centers, companies focusing on innovation as well as new knowledge-based companies. It includes 15 Science & Technological Parks, mainly concentrated in the Barcelona area, of which three are specifically dedicated to biomedicine and three to agro-nutritional R&D and innovation activities.³¹

Table 7

Infrastructure in Biotechnology

Cluster	Country	Total companies	Research Centers	Industrial Associations	Incubators & Science Parks
Aarhus	Denmark	29	4	1	2
Atlantic biotherapies	France	31	7	1	2
Biodundee	United Kingdom	16	4	5	4
Region Munich	Germany	170	6	2	3
Umea	Sweden	26	3	1	2
Biovalley	Germany/France/ Switzerland	30	6		12
biotechvalley.nu	Sweden	16	3	3	1
Cambridge	United Kingdom	422	13	1	13
Ile de grance	France		29	4	12
Grenoble alpes	France	14	14	1	3
Heidelberg	Germany	121	8	4	3
MI-TO	Italy	114	25	4	6
Szeged neurobiologic.	Hungary	7	3		0
Uppsala	Sweden	37	6	1	2
Vaccione therapy	Hungary	3	4	0	0
Catalonia	Spain	41	15	1	6

Source: Netbioclue, Dos and don'ts for biotech cluster development / author.

4. Conclusions

Biotechnology is rapidly gaining priority in many countries as a key engine for long-term economic growth. This is also the case of Catalonia, which now has the largest share (23.7 percent) of firms with activities related to biotechnology in Spain (Asebio, 2007).

There is no doubt of the relevance of Catalan biotechnology within the Spanish context. However, in order to be able to evaluate the Catalan competitive strengths and weaknesses in biotechnology, one should take a more international perspective and compare the position of Catalonia to that of other biotechnology regions. In the international context the United States is clearly the leader, with an already maturing biotechnology sector and, hence, with firms that have quite different characteristics and needs from the Catalan ones, which are only in the early stages of the development of the sector. Because of this, when looking at the competitive position of the Catalan biotechnology, we have focused on the comparison of Catalonia with

³¹ Xarxa de Parcs Científics i Tecnològics de Catalunya - XPCAT web.

the most active European bioclusters (Munich, Oxford, Cambridge) as well as with some more recent ones (Flanders).

We can conclude the following: first, the biotechnology sector in Catalonia is still small by European standards, with an average of only 17 workers per firm and only 41 pure biotech companies. However, it is quickly catching up. In 2006, for instance, Catalonia was the most dynamic Spanish region in biotechnology.

Second, the Catalan effort in research has been improving steadily and, for some disciplines such as biochemistry, it has overcome the position of other European biotechnology regions. However, in patents and licensing, the distance from Europe remains still very high.

Third, red biotech accounts for more than two thirds of the Catalan biotechnology firms. This is not so surprising if we take into account the fact that more than 70 percent of the Spanish fine pharmaceutical production is located in Catalonia. However, Catalonia also boasts 40 percent of all the chemical production in Spain and only 12 percent of the Catalan biotech firms are devoted to white biotechnology.

Fourth, one of the main advantages of the Catalan biocluster relies on the attractiveness of Barcelona to draw key staff (having been ranked as the business city with the best quality of life in Europe. However, researcher salaries are still below the European average).

Fifth, access to funding still remains an important challenge for the Catalan biotechnology firms. Part of this could be due to the following two facts: the average size of the related industries is relatively small compared to the size of industries hosted in other European biotechnology clusters. These firms are the ones that have the capacity to generate demand for biotechnology in several intermediate stages of the value chain production process and such a demand is eased by proximity. The second fact is that the potential investors are not familiar with this type of investment (high uncertainty and long value chains). However, this last aspect has considerably improved recently with the constitution of several Spanish venture capital firms exclusively focused on biotechnology.

Sixth, the main challenge now is to find funding sources for those firms that have already been in the market for a while and which could be facing a “finance precipice”. This is particularly true in the current economic environment.

Given this evaluation, we propose the following three policy recommendations:

First, policy should focus on providing the right incentives to promote quality research and on facilitating the implementation of such research into a business model, regardless of the particular sector it involves.

Second, policy should help foster management and staff mobility. The size of related firms from which biotechnology could attract managers is quite small in Catalonia, compared to European ones. Biotechnology firms might need to look outside, not only for managers, but also to attract key researchers. Staff mobility from one biocluster to another also has the additional advantage of potentially helping attract more international capital. Catalonia could, in this way, obtain managers that have experience abroad and that might already have a track record of attracting foreign venture capital.

Third, policy should contribute to fostering the understanding of the biotechnology sector as another way of helping to attract investors. The Catalan biotechnology sector needs to be

creative in finding ways to attract not only foreign but also national capital. One way is to facilitate the understanding of the sector characteristics amongst potential investors: long timelines, high uncertainty but also high potential. Moreover, often, when one invests in biotechnology, the investment is not on the development of a final product but on achieving the next step in the value chain (i.e., reaching phase I of the clinical trial) and hence, the relevant timeline for the investment might end up being shorter than initially expected.

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Appendix A

Quantifying the Potential Impact of Catalan Biotech. Sector Values by Concept

Biotech sector	CCAIE Name	CCAIE equivalence	Idescat smallest sector data provided	Labour force 2001 (thousands)	Labour force 2006 (thousands)	% Labour force Variation	GVA m.p. 2001 (thousands)	GVA m.p. 2006 (thousands)	% GVA m.p. Variation
Human Health	Pharmaceuticals	244	244	20.7	19.9	-3.9%	1,538,092	1,752,295	13.9%
Primary prod. & Agro-food	Agriculture, hunting and forestry	A	A+B	73.0	87.28	19.6%	2,283,000	2,613,000	14.5%
Primary prod. & Agro-food	Fishing	B							
Primary prod. & Agro-food	Manufacture of food products and beverages	DA 15	15.16	76.1	78.2	2.8%	3,798,960	4,345,027	14.4%
Primary prod. & Agro-food	Manufacture of fertilizers and nitrogen compounds	DG 24.15	Inside Chemistry industries	Inside Chemistry industries	Inside Chemistry industries	Inside Chemistry industries	Inside Chemistry industries	Inside Chemistry industries	Inside Chemistry industries
Primary prod. & Agro-food	Manufacture of pesticides and other agro-chemical products	DG 24.2	Inside Chemistry industries	Inside Chemistry industries	Inside Chemistry industries	Inside Chemistry industries	Inside Chemistry industries	Inside Chemistry industries	Inside Chemistry industries
Primary prod. & Agro-food	Manufacture of pharmaceuticals, medicinal chemicals and botanical products	DG 24.4	Inside Human Health	Inside Human Health	Inside Human Health	Inside Human Health	Inside Human Health	Inside Human Health	Inside Human Health
Primary prod. & Agro-food	Manufacture of other chemical products	DG 24.66	Inside Chemistry industries	Inside Chemistry industries	Inside Chemistry industries	Inside Chemistry industries	Inside Chemistry industries	Inside Chemistry industries	Inside Chemistry industries
Primary prod. & Agro-food	Technical testing and analysis	KA 74.30	74.30	5.0	8.1	61.8%	189,258	293,828	55.3%
Primary prod. & Agro-food	Veterinary activities	NA 85.20	No data	1.6	Missing data	25.9%	32,942	Missing data	
Industrial	Chemistry industry (without Pharmaceuticals)	24 without 244	24 without 244	41.7	40.9	-1.9%	2,789,456	3,724,228	33.5%
Industrial	Manufacture of textile and textile products	17	17	60.2	36.3	-39.7%	2,777,482	1,410,034	-49.2%
Industrial	Manufacture of wearing apparel; dressing and dyeing of fur	18	18	32.8	19.9	-39.3%	907,498	751,229	-17.2%
Industrial	Manufacture of leather and leather products	19	19	5.5	3.7	-32.7%	204,744	129,385	-36.8%
Industrial	Manufacture of pulp, paper and paper products	21	21	18.8	18.2	-3.2%	1,018,648	1,153,738	13.3%
Industrial	Manufacture of coke, refined petroleum products and nuclear fuel	23	101-120 and 23	1.2	1.4	16.7%	1,070,758	3,487,865	225.7%

Appendix B

Quantifying the Potential Impact of Catalan Biotech. Sector Values by Concept

Table B.1

Products & Services launched to market in 2007 by Catalan Companies		
Company	Product	Type
Advancell	Evaluation of substances subject to the REACH normative	Research Service
Neuroscience Technologies	Microneurography Test in patients with neuropathic pain	Research Service
Neuroscience Technologies	Microneurography test in animal model (rat)	Research Service
Thrombotargets	BioplatformScreen	Research Service
IUCT	GC-BIO-DF	Pharmaceutical Active Ingredient
IUCT	GC-BIO-F	Pharmaceutical Active Ingredient
IUCT	GC-BIO-TFF	Pharmaceutical Active Ingredient
IUCT	GC-BIO-DT	Pharmaceutical Active Ingredient
IUCT	GC-BIO-DAP	Pharmaceutical Active Ingredient
IUCT	IUCT-S50	Biofuel

Source: Asebio, Selected companies are author's selection based on headquarters location.

Table B.2

Main financial operations in the Spanish biotechnology sector in 2007 involving Catalan biotech companies			
Company	Investor	Concept	Investment (m€)
Ab Bcn	CDTI NEOTEC No Disponible	NEOTEC	N/A
Advancell	Ceosa, Talde, A.Vila Casas, Unisco, BCN Empren y otros	Capital Increase	7.5
Advancell	CDTI	Loan	2.4
Agrasys	CDTI	NEOTEC	N/A
Era Biotech	BCN Ventures	Capital Increase	0.3
Genmedica Therapeutics	Uninvest-Unirisco	Capital Increase	0.8
Genmedica Therapeutics	BCN Ventures	Capital Increase	0.8
Infinitec Activos	BCN Ventures	Capital Increase	0.05
Microbial	CDTI	NEOTEC	N/A
Neuroscience Technologies	CIDEM	Loan	N/A
Neuroscience Technologies	CDTI	NEOTEC	0.32
Neuroscience Technologies	Private partners	Capital Increase	0.14
Omnia Molecular	CDTI	NEOTEC	N/A
Thrombotargets Europe	Biotech Angels	Capital Increase	2
Thrombotargets Europe	Biolead Capital	Capital Increase	2
Thrombotargets Europe	ENISA	Capital Increase	0.6
Uni-Biofocus	Caixanova	Fund participation	6

Source: Asebio. Annual Report 2007. Selected companies are Author's selection based on the head offices location.

In United States and United Kingdom, the currency symbol goes before the quantity. Therefore, Table B.2, last column "Investment (m€)" – should read "Investment (€m)."

Also, last line should read "head office location", not "head offices."