Success and failure in the development of biotechnology clusters: the case of Lombardy

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1. *Introduction*

This paper discusses the development of the biotechnology industry in an Italian region, Lombardy. More specifically, it asks why significant innovative and commercial activities in biotechnology did not emerge in what might have been considered at the outset a promising area for the growth of this industry and why in very recent years some timid symptoms of dynamism seem to be appearing.

As a case-study about a failure, rather than a success story, it is difficult to draw firm conclusions. In a sense, the problem is overdetermined. There are too many possible candidate variables that might explain why innovative activities in biotechnology did not take off and available data do not allow any serious statistical test.

As a consequence, the paper is largely speculative. However, we shall try to make some steps forward in turning speculation into an appreciative account, based on a theory-driven interpretation of the determinants of the patterns of innovative activities in specific geographical areas.

There is now considerable empirical evidence that innovative activities tend indeed to cluster in specifix geographic area, at dfifferent levels of aggregation (Audretsch and Feldman 1996, Feldman 1994, Krugman 1991, Swann, Prevezer and Stout 1998). The case of biotechnology is extreme and puzzling, in this respect, from a variety of perspectives. First, it is very well known that the biotechnology industry is largely an American phenomenon and that other countries have been lagging behind for over two decades. Despite some recent encouraging signals of dynamism in some European countries and in Japan, the American leadership is still undisputed. Even within the USA, the development of biotechnology has been characterized by high degrees of regional concentration. In Europe too innovative activities in biotechnology tend to agglomerate into specific areas. So, what are the factors that explain different performances in “national biotech”? And what are the factors leading to agglomeration in the case of biotechnology?

After an overview of the patterns of development of biotechnology in Italy (Section 2), the specific case of the biggest biotechnology cluster in Italy – Lombardy - will be described (Section 3). Then, I shall briefly touch upon two main conceptual issues which have attracted in recent years the attention of many analysts and which drive this paper too. Namely:

a) what are the factors that might explain the lagging behind of the Italian (and more generally, European) biotechnology industry vis-a-vis the United States? (Section 4)
b) Do innovative activities tend to cluster in specific geographical areas? If the answer is positive, what are the determinants of these processes of agglomeration, at least in the case of Lombardy? (Section 5).

2. The background: the development of biotechnology in Italy

In Italy, as in other European countries, innovative activities in biotechnology lagged significantly behind the USA and proceeded along different lines. Structural weaknesses in the industrial base, in the research system and at the institutional level hindered the development of biotechnology.

The main difference, of course, is the virtual absence of the phenomenon of the specialized biotechnology startups, even as compared to other European countries. No reliable figure of the number of new biotechnology firms is Italy is available, but a rough estimate would suggest that they are around less than two dozens. Moreover, the few Italian start-ups do not resemble the American prototype under many respects. Most of them are not involved in drug research or development but are instead either intermediaries commercializing products developed elsewhere, or in the provision of instrumentation and/or reagents. Finally, some of these companies (especially the most significant ones) have been founded as spin-offs of larger pharmaceutical companies undergoing processes of restructuring rather than as University spin-offs. However, the major distinctive feature of the Italian case is the delay with which innovative activities got started and the limited size and scope of such efforts, even within the large chemical and pharmaceutical (and agro-food) companies. Even today, Italy has to be considered a background country in biotechnology. Just to give a rough idea, it is worth noting that the number of Italian patent applications to the European Patent Office totals to only 163 in the whole period 1978-1996.

In the absence of extensive new firm founding, most of the innovation in biotechnology in Italy - as in other countries of mainland Europe - has occurred within established firms and public research centers . The main actors in the development of biotechnology in Italy were the large chemical firms and the beginning of research activities, as well as the emergence of public policy, was contextual to the formation of a “biotechnology lobby”, who stimulated the interest of industry and above all of the government. By the early Eighties, the two largest Italian chemical groups – ENI and Montedison - had already started some small research activities and had considered the possibility of some more systematic effort. However, such plans resulted only in the establishment of two small research agreements with Italian academic laboratories. Besides ENI and Montedison, only a handful of medium-sized pharmaceutical companies engaged in innovative activities, whilst the absence of any research tradition in the food industry and in agriculture prevented any significant effort in those directions.

Around the chemical industry, however, a biotechnology lobby gathered and organized. Scientists were the first to perceive the potentialities of biotechnology and took an active role in eliciting both industrial and public interest in the new emerging techniques. Yet, they had traditionally only few linkages with industry and their pressure achieved some results only when they succeeded in involving the Association of the Chemical Industry (Federchimica). Federchimica was perhaps the single most influential institution in the development of Italian biotechnology. In 1986, it published the first major report on biotechnology and from then on it lobbied for getting public support. Subsequently, Federchimica spun off other initiatives, particularly the Italian Biotechnology Industrial Association, although its main result was to elicit and contribute to design government intervention.

The weakness of government support is a further distinguishing feature of the Italian case. Before 1986, public support to biotechnology was very small and uncoordinated. It flowed mainly to universities through the National Research Council's (CNR) "Finalized Projects", but research funding was small and it was spread over many diverse and very general projects, without any clearly defined priority. Industry was only marginally involved in these projects. Industrial research was funded through the two existing schemes supporting applied research, but again no specific priority was attributed to biotechnology.

Like in most countries, the Italian government agencies knew very little about biotechnology and, given the uncertainty surrounding its future developments, they weren't able to devise any specific policy. Differently, from other experiences, though, the Italian administrative apparatus lacked also the experience, the competencies and the structures for dealing with the problems of formulation and implementation of a set of policies in high tech industries (Orsenigo, 1989). Thus, the existence of biotechnology was not even perceived until the mid 1980's, under the pressure of the biotechnology lobby and of the example coming from other countries.

Attempts to coordinate interventions and to devise a coherent strategy started only in the second half of the Eighties, when a National Committee for Biotechnology was established at the Ministry for Scientific and Technological Research (MURST). The Committee comprised the scientists and the industrialists of the original biotechnology lobby and eventually designed the National Plan for Biotechnology, which was passed by the Parliament in 1987.

The plan was aimed at supporting applied research in different fields (especially biomedical research), while support to basic research and industry-university collaboration was provided through new programs launched by the CNR Other initiatives were taken to stimulate research conducted in the public research centres like ENEA and the CNR. In the following years other programs were launched by the CNR, by MURST, and other Ministries. It is very difficult to evaluate the effective size of the financial resources devoted to the support of (basic and applied) research and to the promotion of industry-university collaboration, let alone the impact of these projects. An extremely rough estimate would suggest that in the period 1987-1996 the total funding amounted to a figure around L. 1.000-1.200 billion. An analysis of the National Research Plans on biotechnology launched by Ministry of University and Scientific and Technological Research in the period 1989-1997 suggests however that only a small group of universities and an even smaller group of companies were involved by these projects, with a very limited scientific output (only 1 patent extended outside Italy) and little interaction between universities and the companies (Cancogni, 1997).

In addition to these initiatives, the development of biotechnology in Italy was characterized by the mushrooming of local collaborative initiatives between public and private agents at the local level, through the establishment of science parks, research consortia, venture capital funds, etc.. However, the scope and the impact of these efforts has remained on the whole quite limited.

Thus, despite these efforts, very few firms engaged in significant research activities and their innovativeness was far lower than that of the major European competitors. Very few firms account for a large proportion of biotechnology patents, and innovation in biotechnology rests essentially on the activities of a small group of large/medium- sized established companies. As a consequence, the Italian performance as a whole remains far behind that of Germany, France, U.K., Switzerland, but also of Sweden and Denmark. (Table 1)[1]

//INSERT TABLE 1 ABOUT HERE //

In the 1980s, the main actors were the two large Italian chemical groups, ENI and Montedison. As far as Montedison is concerned, research capabilities in biotechnology were present in the laboratories of Farmitalia-Carlo Erba, its pharmaceutical subsidiaries and the largest and more prestigious Italian pharmaceutical company at the time and in the central laboratories of the group (Istituto di Ricerche Donegani). In the late 1980s, Montedison expanded its biotechnology research through acquisitions and through the development of a network of collaborations with domestic universities and American laboratories and specialized biotechnology firms.

[1] Another indicator of the scarce involvement of Italian industry in biotechnology is given by the participation to the National Association for the Development of Biotechnology (Assobiotec), the trade association created within the Chemical Industrial Association in 1986. The total number of participating firms peaked to only 58 in 1992 and subsequently it has been declining. Clearly, not all the firms involved in biotechnology participate to the Association and over the last few years divergences within the Association have led some companies to retire their membership. On the other hand, very few of these companies do actually perform research, but they are mainly involved in the commercialization of products and serviced generated elsewhere. An independent survey on the Italian biotechnology industry carried out in 1989 showed that out of the 134 companies identified by Federchimica as being involved in biotechnology research, only 20 of them had actually in place some ongoing research. The total R&D expenditure of these companies was estimated to be around L.200 billion, including also expenditures not directly linked to research proper, like salaries paid to all the employees in specialized firms (Orsenigo, 1991).

As for ENI, a significant biotechnology group was created within EniRicerche (the research labs of the group). Moreover, ENI owned Sclavo, a medium sized company located in Siena, considered to be among the world leaders in vaccine production.

Finally, a subsidiary of the Fiat group, Sorin, active in the production of medical devices, started research on the development of diagnostic kits based on the use of monoclonal antibodies and assays.

Since the beginning of the Nineties, however, even these initiatives were drastically downsized. The Italian chemical and pharmaceutical industries underwent a deep crisis. The Italian chemical and pharmaceutical companies were already structurally weak, small on international standards and their commitment to innovative activities was certainly not comparable to that of their international competitors. The major Italian chemical and pharmaceutical companies were acquired by foreign corporations. Now, more that 70% of total pharmaceutical sales on the Italian market are generated by foreign-owned firms and by subsidiaries of large multinationals. Moreover, a series of scandals linked to the diffusion of a bribery system in the processes of determination of the prices of drugs, hit severely the industry in the early Nineties. Finally, cost containment policies by the Government implied a further shock on the profits and on the strategies of the pharmaceutical companies operating in Italy.

As a consequence, investments on biotechnology R&D were drastically reduced. For example, the pharmaceutical division of Montedison – Farmitalia Carlo Erba - was eventually acquired by Pharmacia and its research activities were subject to substantial processes of restructuring. Similarly Sclavo (now called Biocine), after a series of break-ups and vicissitudes, was acquired by Chiron. Many research projects were discontinued and – given the overall weakness of Italian research capabilities - only few initiatives were launched or maintained by the foreign research headquarters to compensate the decrease of domestic investments.

3. The development of biotechnology in Lombardy

The history of the development of biotechnology in Lombardy coincides to a very large extent with the history of Italian biotechnology as a whole. Indeed, since its inception, innovative activities in this area have been strongly concentrated in few regions, Lombardy being by far the single most important center, followed by Tuscany and – in the Nineties – by Latium. Lombardy accounts for almost half (43.9%) the patents applied for to the European Patent Office in the period 1979-96 and its contribution has been only slightly declining in the period 199-96 (falling to 39.4%). Jointly, Lombardy, Latium and Tuscany contribute to around 80% of total Italian patenting activities[2] and over the past few years the overall degree of spatial concentration of innovative activities in biotechnology has changed very little[3].

The agglomeration of innovative activities in Lombardy– and more specifically the area around Milan – might be simply explained by the fact that Milan had the strongest concentration of research laboratories, both academic and industrial, and it was by far the major financial center of Italy.

Milan was traditionally one of the major centers of academic research in medicine and in biology. Whilst other universities had perhaps the best research teams and the more advanced "schools", yet in Milan one could find a very strong concentration of units and researchers in different disciplines.

In Lombardy, was located traditionally the large majority of the chemical and pharmaceutical industry and especially their headquarters and their research labs[4]. More generally, Lombardy shows consistently over time a very strong technological specialization in chemicals and pharmaceutical, whichever indicator is used (R&D expenditures, patents, number of researchers, etc.).

At the beginning of the Nineties, Lombardy hosted 49% of the Italian firms active in biotechnology, 36.3% of the researchers in industry and 42.6% of the research laboratories. Similarly, Lombardy attracted 29% of the public funds made available by the National research Council's "Finalized Project" on Biotechnology. It is also worth noting that, respectively, more than three quarters and around 60% of all the collaborations among firms – both at the national and international level – and universities in biotechnology involved companies (universities) located in Lombardy (Orsenigo, 1991).

Against this background, a series of initiatives were taken to further develop biotechnology research and commercial activities, primarily through the creation of science parks or – more

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[2] The Tuscany clusters reflects the strong position of Siena, where there is considerable tradition in biomedical scientific research at the university and where Biocine (formerly Sclavo) is located. Conversely, Latium is the location of the headquarters of several multinational companies and thanks to public subsidies several research laboratories have been opened in Pomezia, just outside Rome.

[3] In this perspective, the Italian case would seem to support the hypothesis that innovative activities (especially in new technologies) tend to exhibit strong tendencies towards the agglomeration in few geographical areas and that spatial concentration tends to persist over long periods of time. In the present case, however, this observation might be simply the outcome of a small numbers problem and - more generally – of the absolute low level of innovative activities in this field in Italy. In other words, spatial concentration might result here not so much from the working of specific agglomeration forces, but simply from the sporadic nature of innovative activities.

[4] In Milan was located Federchimica. Montedison had its headquarters in Milan and its main research laboratories (Istituto Donegani) were located in the neighborhood (although in a different region Piedmont). Similarly, the main research laboratories of ENI, EniRicerche was located just in the outskirts of Milan.

generally- aggregations of academic and industrial researchers to promote collaborative research and act as incubators for academic spin-offs.

The first initiative was the so-called "Biopolo", a consortium between a few pharmaceutical companies and academics of the Faculties of Biology, Chemistry and Agricultural Sciences, with the participation – under various headings – of the local authorities. The Biopolo was an offspring of the original "biotechnology lobby" and was promoted and stimulated by a group of professors of the State University of Milan since the late Eighties. Its main area of interest was the applications of biotechnology to the agrofood industry and environment.

In practice, the Biopolo took off very slowly, as a consequence of the scandals in the pharmaceutical industry, political meddling and academic politics. Its main activity consisted in supporting the creation of the a specific field denominated "biotechnology" within the Faculty of Sciences in the State Milan University and collaboration between university and industry was essentially focussed on teaching activities and training. Only recently, with the creation of the 2nd State University of Milan in 1998 – resulting from the splitting of the previous institution – the Biopolo has started operating in a more systematic way. With the creation of the 2nd University, in fact, a Faculty of Biotechnology was started which is beginning to act as a center of aggregation for research.

A second initiative, the S. Raffaele Science Park, was more successful. The Science Park was launched in 1993 under the impulse of the boss of the S. Raffaele hospital, a private institution created and managed by a charismatic (and highly controversial) priest/entrepreneur, Don Luigi Verzè. The San Raffaele Hospital was conceived and developed putting a high priority on research – particularly on biotechnology and in general on molecular biology - and it quickly became a leading scientific center in the biomedical area in Italy, with solid relationships with the international community and high quality standards and reputation. Around the S. Raffaele Hospital, DIBIT (Department of Biological and Technological Research) and subsequently the S. Raffaele Science Park were formed, initially without any public funding. Now, the Science Park hosts 63 research units, including also laboratories of the National Research Council, of the Polytechnic of Milan, and since last year of the new University "Vita e Salute" (another initiative of Don Verzè, with Faculties of Medicine and Psychology and conceived as a highly prestigious and selective institution). A number of important international pharmaceutical companies and a couple of new start-ups (which are not yet completely operative, though) participate to the S. Raffaele Science Park, with specialized laboratories in a large variety of research areas. Moreover, the S. Raffaele Science Park hosts also a number of laboratories funded by initiatives like Telethon and by other private foundations.

Although the S. Raffaele Science Park has among its main objectives the promotion and the assistance to spin-offs, with the provision of various types of services (scientific, technological, logistical financial and administrative services), no really important result has been achieved so far in this area.

Actually, the most important and notable examples of new biotechnology companies in Lombardy are not university spin-offs, but industrial spin-offs, born out the processes of restructuring of some large pharmaceutical companies.

One of these cases was Lepetit, leader in antibiotics research and production. After being acquired by Marion Merrel Dow, its laboratories had become one the major research centers in this field. After a series of vicissitudes, however, Lepetit was finally acquired by HMR and the lab was closed. At this stage, a group of researchers took the initiative to launch a new company, Biosearch Italia, trying to maintain and exploit the accumulated know-how. With the support of venture capitalists (3i Investor in Industry), the new company was founded with the aim of being quoted in the newly created "Nuovo Mercato (the equivalent of the Neuer Markt or the Nouveau Marché) within the year 2000. Its main research lines are focussed on antibiotics, but new areas have also beeen opened in anti-tumorals and genomics, in collaboration with the former parent company, now Aventis.

A similar story is that of Newron. Here, once again, a group of researchers from Pharmacia & Upjohn (formerly Farmitalia – Carlo Erba) of the R&D labs near Milan decided to continue their research with funding from 3i in the area of the central nervous system after the closure of their lab. Initially, they are hosted by Biosearch Italy, renting some spaces and services by them. Newron is expected to be quoted on the Nuovo Mercato in three years time.

NovusPharma is a further example, being born from the restructuring processes of the Boehringer Mannheim branch operating in the area of oncology. After the acquisition from Hoffman La Roche, the labs were closed. In this case, three European venture capital firms (the Italian branch of 3i, Atlas Ventures (NL) e Sofinnova (F)) support the initiative of some researchers to create their own company. NovusPharma has already developed collaborations with the National Institue on Tumours, the European Institute of Oncology and the Faculty of Biotechnology of the 2nd University of Milan and maintains an agreement with Roche. NovusPharma has ambitious growth targets and quotation on the Stock Exchange is expected in two years time.

4. Discussion: factors explaining the (slow) development of biotechnology in Italy and the case of Lombardy

To a large extent, explanations of the feeble development of biotechnology in Italy, of the clustering of innovative activities in Lombardy and in few other areas and of the specific evolution of the industry in Lombardy tend to coincide. We would also advance the hypothesis that the Italian case is just an extreme instantiation of the more general European experience.

To deal with this questions, however, one has to distinguish among two different issues. First, why didn' t NBFs flourish in Europe? Secondly, why European large established companies were – in general terms – slower as compared to their American counterparts in adopting biotechnology – more precisely molecular biology?

4.1 Factors hindering the development of new biotechnology companies

It is now widely recognized that in the United States a combination of factors made it possible for small, newly founded firms to take advantage of the opportunity created by biotechnology. In Europe (although to a lesser extent in the U.K.) many of these factors were not in place. Let us quickly examine the role of these factors in the case of Europe and Italy in particular.

4.1.1 Strength of the local scientific base

It is widely recognized that the very strong state of American academic molecular biology played an important role in both facilitating the proliferation of startups (Sharp, 1985, Orsenigo,1989, Zucker, Darby and Brewer, 1997). The strength of the local science base may also be responsible, within Europe, for the relative British advantage and the relative German and French delay. There seems to be little question as to the superiority of the American and British scientific systems in the field of molecular biology, and it is tempting to suggest that the strength of the local science base provides an easy explanation for regional differences in the speed with which biotechnology developed.

In Italy, it is widely acknowledged that the level and the scope of basic research in molecular biology was not very high. Indeed, some research groups conducting state-of-the art research were present in the early Eighties, especially in fields like immunology. Naples and Pavia were particularly important in this respect. In Naples, IIGB (International Institute of Genetics and Biophysics), which was directed for a few years during the 1960s by James Watson, was an internationally renowned research center that spun off successive generations of high quality researchers and clusters of research groups spread all over Italy. Similarly, Pavia constituted another pole of excellence, where Italian studies in genetics were practically born thanks to the work of Buzzati Traverso and where subsequently an important National Research Council group was created and developed. Milan and Rome had also some excellent research groups, whilst Genua had a tradition of research in immunology and IST (Institute for Research on Tumours), a spin-off of the National Institute for Cancer Reasearch) was created. Padua, finally, had developed instead significant competencies in the field of the chemistry of proteins.

Other research initiatives were developed within public research centres (like the CNR's groups or ENEA5) and by private institutions. For example, the Italian Association for Cancer Research (mainly a funding agency) introduced a new, competitive approach to the funding of scientific research in Italy. The National Institute for Cancer Research and its offspring IST (Institute for Research on Tumors in Genoa) operated at the frontier of knowledge in experimental oncology and in immunology and had a dense network of relationships with American and British laboratories. Moreover, they started since the mid Eighties a systematic attempt to slow down the brain drain process that was hitting the domestic research system by recruiting expatriated Italian researchers. The Mario Negri Institute for Pharmacological Research, which was initially located in Bergamo and then opened up various branches in other locations, was another center of excellence in research.

In sum, while some good research centers existed, yet on the whole Italian research in molecular biology and in other disciplines relevant to biotechnology was lagging behind most of the major European countries. Above all, research was concentrated in few heterogeneous clusters, with little communication and coordination except personal and informal relationships among the individual researchers. Over the years, the level and the scope of basic research have significantly improved, thanks also to the activities and the international contacts of a younger generation of researchers who studied and worked initially in the USA and other countries, but they still lag significantly behind the main European countries in terms of absolute amounts of funding, organizational efficiency and overall quality of the research.

The strength of the local knowledge base goes also a long way to account for the agglomeration of innovative activities biotechnology in few clusters in Italy. However, some qualifications are needed. First, as we have seen, Milan did not necessarily have the best scientific research in absolute terms as compared to other Italian locations. Second, centers which had poles of excellence in scientific research did not become important biotechnology clusters, e.g. Naples. This would suggest, at this stage, that not only the absolute quality of science, but also the existence

[5] ENEA was the Agency for research on nuclear technologies.Its mission changed several times after the decision to stop nuclear research in Italy and became successively an agency for research in alternative energy sources and a center for coordinating technology transfer).

of critical thresholds in the "quantity" of good science were necessary conditions for the emergence of clusters.

4.1.2 Industry-university relations

An explanation based only on the strength of the local scientific base might seem unsatisfying to the degree that academic science is rapidly published and thus, in principle, rapidly available across regions and across the world. However, even in this extreme case of a science-based technology, in the early years of the industry the exploitation of "biotechnology" required the mastery of a considerable body of tacit knowledge that could not be easily acquired from the literature (Zucker, Darby and Brewer, 1997; Pisano, 1996, Orsenigo, 1989).

Thus, it has often been suggested that the flexibility of the American academic system, the high mobility characteristic of the scientific labor market, the willingness to exploit the results of academic research commercially[6] and, in general, the social, institutional and legal context that made it relatively straightforward for leading academic scientists to become deeply involved with commercial firms were also major factors in the health of the new industry.

In contrast links between the academy and industry -- particularly the ability to freely exchange personnel -- appear to have been much weaker in Europe. Indeed, the efforts of several European governments were targeted precisely towards the strengthening of industry-university collaboration.

Thus, one observes a mushrooming of initiatives all across Europe aiming at establishing stronger links between industry and universities and to encourage a more entrepreneurial attitude by universities. In practice, policies have been targeted mainly to the set-up of specific organizational devices to manage technology transfer, like science and technology parks or other agencies for technology transfer. These initiatives have taken a wide variety of forms and show a mixed record in their performance.

In the case of Italy, certainly the structure and the norms governing the academic system did not favour the entrepreneurial exploitation of university-based research. Interactions between industry and university had been traditionally weak and in any case largely informal and based on personal – rather than institutional – relations.

This state of affairs has changed very slowly over the years and it has been only in very recent times that symptoms of the diffusion of a different attitude have started to emerge. In a survey carried out in 1994 among the academic researchers participating to the National Plan for Biotechnology – a program launched by the Ministry of University and Scientific and

[6] This willingness has been strengthened since the late 1970s with the passage of the Bayh-Dole Act.

Technological Research (MURST) to sustain biotechnology research and industry-university collaboration – a large fraction of the respondents to the questionnaire declared themselves willing to engage more directly in the commercial exploitation of their research. However, administrative rules and the lack of appropriate organizational structures within the universities were quoted as the main factor hindering such developments (Cesaroni, Cioppi and Gambardella 1995). A more recent study on industry-university relations in Italy (Orsenigo and Cancogni, 1999) confirmed that, despite a renewed dynamism in this field, only few universities have developed any systematic organizational structure to deal with relationships with industry and with the commercial exploitation of scientific research. More than 60% of universities does not even have standard contract typologies, let alone dedicated technology transfer offices.

Thus, the traditional separation between academia and industry and the organizational deficiencies within universities made it very difficult to commercialize academic research. However, it has to be stressed that, given the weakness of scientific research in general, the absence of appropriate "transfer mechanisms" appears to have played so far a relatively minor role. To put it provocatively, transfer mechanisms are largely irrelevant if there is nothing to be transferred. Moreover, the development of organizational structures supporting technology transfer appears to be itself largely dependent on the existence of a strong research base.

4.1.3 Access to Capital

It is commonly believed that lack of venture capital restricted the start-up activity of biotechnology firms outside the U.S. Clearly, venture capital played an enormous role in fueling the growth of the new biotechnology based firms, (or "NBFs"). However, at least in Europe, there appear to have been many other sources of funds (usually through government programs) available to prospective start-ups. In addition, the results of several surveys suggest that financial constraints did not constitute the main obstacle for the founding of new biotechnology firms in Europe (Senker 1998). In addition, although venture capital played a critical role in the founding of U.S. biotechnology firms, collaborations between the new firms and the larger established firms provided a potentially even more important source of capital. Yet, European large companies tended to collaborate relatively more with U.S. biotechnology firms, rather than with prospective European start-ups [7]. Even in the absence of other institutional barriers to entrepreneurial ventures, start-ups in Europe might have been crowded out by the large number of U.S. based firms anxious

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[7] Indeed, most NBFs' strategies emphasized licensing products rights outside the U.S. to foreign partners. Thus to an even greater extent than many established U.S. pharmaceutical firms, European firms were well positioned as partners for U.S. NBFs.

to trade non-U.S. marketing rights for capital (Henderson et al., 1999). Given the number of U.S. NBFs in search of capital, European firms had little incentive to invest in local biotechnology firms.

As a partial support to this interpretation, in Italy several initiatives by both domestic and foreign investors to launch venture capital funds were attempted in the Nineties, with little success so far. These funds, if anything, ended up investing in new biotechnology companies outside Italy. Conversely, some of the few experiences of successful Italian NBFs have been funded by foreign venture capital firms. Thus, the failed development of venture capital in Italy seems to depend less on the lack of investors and funds than on the paucity of supply of promising startups based on solid scientific research.

4.1.2 Intellectual property rights

It is widely acknowledged that the establishment of clearly defined property rights also played a major role in making possible the explosion of new firm foundings in the US, since the new firms, by definition, had few complementary assets that would have enabled them to appropriate returns from the new science in the absence of strong patent rights (Teece, 1986).

In the USA, a very tight appropriability regime in the biotechnology industry emerged quite quickly. In 1980, the Congress approved the so-called Bayh-Dole Act, which gave universities (and other non-profit institutions, as well as small businesses) the right to retain the property rights to inventions deriving from federally-funded research[8]. In 1980, the US Supreme Court ruled in favor of granting patent protection to living things (Diamond v. Chakrabarty), and in the same year the second reformulation of the Cohen and Boyer patent for the rDNA process was approved. In the subsequent years, a number of patents were granted establishing the right for very broad claims (Merges and Nelson 1994). Finally, a one year grace period was introduced for filing a patent after the publication of the invention.

In Italy, as in Europe as a whole, the grace period introduced in the USA is not available: any discovery that has been published is not patentable. Moreover, the interpretation has prevailed that naturally occurring entities, whether cloned or uncloned, cannot be patented. As a consequence, the scope for broad claims on patents is greatly reduced and usually process rather than product patents are granted. A draft directive from the Commission that attempted to strengthen the protection offered to biotechnology was approved by the European Parliament only in 1998, and an earlier version was rejected in 1994. Still, considerable controversy surrounds this issue.

8 The 1984 passage of public Law 98-620 expanded the rights of universities further.

While it is clear that stronger intellectual property protection is not unambiguously advantageous, it is however highly plausible that at least in the early days of the industry the U.S. reaped an advantage from its relatively stronger regime.

4.1.3 A regulatory climate that did not restrict genetic experimentation

Opposition to genetic engineering research by the "Green" parties is often quoted as an important factor hindering the development of biotechnology, especially in Germany and in other Northern European countries, and public opposition to biotechnology is said to have been a factor behind the decision of some companies to establish research laboratories in the USA. In Italy, these oppositions were not, however, an important factor, at least until last year when systematic opposition to genetically modified food started to develop among consumers.

4.2 Factors hindering the adoption of biotechnology among large established firms

A further important feature of the patterns of development of European biotechnology is the lagged response of many large established companies to adopt the new techniques as compared to American (and to some extent to British) companies. The relevance of this factor can hardly be underestimated. Given the low rate of creation of new start-ups, the development of biotechnology in Europe rested on the activities of large companies. The delay in the adoption of molecular biology within large corporations was therefore an essential factor explaining the European sluggishness. Moreover, in the absence of a vibrant research activity by large firms, new prospective start-ups lacked an essential source of survival and growth, through the establishment of collaborative agreements. As mentioned previously, in the absence of such competencies, large companies would turn to the American scientific and technological base to tap and absorb the new requisite competencies during their catching-up process. Thus, in Europe a vicious circle between the relative backwardness of large firms and low rate of formation of new startups was created.

4.2.1 Firms' size, market structure and the competitive environment in Europe

The rate of adoption of molecular biology by established companies varied widely across the world and across firms. Within Europe some large British and Swiss firms were able to adopt the technology rather quickly. Other firms that had smaller research organizations, that were more local in scope or that were more orientated towards the exploitation of well established research trajectories[9] found the transition more difficult (Henderson and Cockburn, 1994; Gambardella,

[9] In short, those firms that had not adopted the techniques of "rational" or "guided" drug discovery

1995). Thus, many of the smaller American companies, and almost all of the established French, Italian, German and Japanese companies appear to have been slower to adopt the new technologies.

The relative strength of the local science base appears to be again an important part of the explanation. American and UK science was more advanced than mainland European: hence the slow diffusion of the new techniques to Continental European pharmaceutical firms. This explanation is not the whole story, though. For example, many Swiss companies established strong connections with the US scientific system, suggesting that geographic proximity as such played a much less important role in the diffusion of molecular biology.

A second possible explanation is that diffusion was shaped by the relative size and structure of the various national pharmaceutical industries. The pre-existence of a strong pharmaceutical national industry, with some large internationalized companies, may have been a fundamental prerequisite for the rapid adoption of molecular biology. In many European countries (particularly in Italy), the industry was highly fragmented into relatively small companies engaged essentially in the marketing of licensed products and in the development of minor products for the domestic markets. However , size or global reach may have been a necessary condition, but the delay of the largest German to adopt these techniques suggest that it was not sufficient.

Thus, the most plausible explanation is that other institutional variables were also important. A possible candidate is the stringency of the regulatory environment. There is now widespread recognition that the introduction of the Kefauver - Harris Amendments had a significant impact in inducing a deep transformation of the US pharmaceutical industry, particularly through raising the cost and complexity of R&D. Partly as a result many US firms were forced to upgrade their scientific capability.

Similarly, Thomas (Thomas, 1994) has suggested that the European country whose leading firms did move more rapidly to adopt the new techniques - Britain – also appears to have actively encouraged a "harsher" competitive environment. Ever since the Sixties, the British system encouraged the entry of highly skilled foreign pharmaceutical firms, and a stringent regulatory environment also facilitated a more rapid trend towards the adoption by British companies of institutional practices typical of the American and Swiss companies: in particular, product strategies based on high priced patented molecules, strong linkages with universities and aggressive marketing strategies focused on local doctors. The resulting change in the competitive environment in the home market induced British firms to pursue strategies aiming less to the fragmentation of innovative efforts into numerous minor products than to the concentration on few important products that could diffuse widely into the global market. By the 1970s, the ensuing transformations of British firms had led to their increasing expansion into the world markets10.

The diffusion of the new technologies varied however not only across *regions,* but also across *firms.* Most of the firms that rapidly adopted the new techniques were large multinational or global companies, with a strong presence, at least as research is concerned, in the USA and generally on the international markets. Zucker and Darby present some evidence that size alone is a reasonable predictor of adoption, at least in the U.S. (Darby and Zucker, 1995). Henderson (1994) and Henderson and Cockburn (1996) have shown that those firms that adopted faster and more efficiently molecular biology had also already adopted the techniques of "rational" drug discovery. By and large these were larger firms that had early developed a "taste" for science and that were able to integrate the new knowledge within the firms. In turn, this was accomplished through a series of organizational changes directed towards building and sustaining tight links to the public research community, essentially through the successful adoption of particular, academic-like, forms of organization of research (Cockburn, Henderson and Scott, 1997, Henderson *et al*., 1999).

Here other institutional factors appear to have been a necessary, albeit not a sufficient condition.

First, it is likely that the Anglo-Saxon forms of corporate governance made it easier for companies to “hire and fire” personnel or rapidly cut non-performing assets, as compared to firms located in “stake-holders” economies such as Germany. In addition to the problem of cutting established research competencies, European companies faced a risk of giving long-term employment to biologists before biology was proven to be successful over the long run11 .

Second, to the extent that the adoption of the new techniques and of the associated academic-like forms of organization of research within companies was faster in companies that had developed early a “taste for science”, it is tempting to suggest that the origin of the American advantage in the use of biotechnology within large corporations as well as in new biotechnology companies lies in the proximity and availability of first rate scientific research in universities and in the closer integration between industry and the academic community, as compared to other countries. One might also speculate that this was - at least to some extent - the result of strongly scientific base of the American medical culture and - relatedly - of the adoption of tight scientific procedures in clinical trials. Through this mechanism, American companies might have to develop earlier and stronger relationships with the biomedical community and with molecular biologists in

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10 The Japanese experience also looks in many respects like that pursued in Europe outside Switzerland and the UK.

[11] I owe this observation to an anonymous referee. A similar argument is suggested by Casper (1999).

particular. Segregation of the research system from both medical practice and from close contact with commercial firms (as in France and possibly in Germany) has been highlighted as a major factor hindering the transition to molecular biology in these two countries (see for instance Thomas, 1994 , Henderson *et al*., 1999, Orsenigo 2000).

5. ***Clustering***

The previous observations might bear some relevance for an understanding of the causes of the formation of (and of the failure to develop) innovative clusters in high technology industry and in biotechnology in particular.

With specific reference to the case of Italy and Lombardy, it is quite clear that most of the factors that account for the dominance of the US industry were simply not in place. Italy lacked a strong scientific base, its industrial base was weak and there was little interaction between industry and universities. Moreover, financial and regulatory contraints have also plausibly hindered the development of biotechnology. Against this background, it is then not particularly surprising that innovative activities tended anyhow to cluster in those regions where at least some of these conditions were present. If anything – as mentioned above – Lombardy (and in part Tuscany in pharmaceuticals) had a stronger industrial base and it was a relatively big center of academic research.

But are these factors sufficient or only necessary conditions for clustering to occur? And which other forces might explain the phenomenon? The question is particularly important in the case of biotechnology, which is usually considered as a strongly-science based technology and as such – at least in principle – in large part abstract and codified knowledge (Arora and Gambradella, 1997). Under these circumstances, knowledge should be in principle available to everybody. So, what forces led to the agglomeration of biotechnology activities in specific clusters?

Part of the answer lies in the observation that mastery of biotechnology required (and still requires) a lot of complementary tacit knowledge. To the extent that the transmission of tacit knowledge is facilitated by geographic proximity (Pavitt, 1994; Jaffe, Trajtenberg and Henderson, 1993; Audretsch and Feldman 1996, Swann, Prevezer and Stout, 1998), clustering may be a likely outcome. However, in the case of biotechnology other authors have suggested that the US startups were not simply the result of geographic proximity (Zucker, Darby and Brewer, 1997, Zucker, Darby and Armstrong, 1998) To put it in a different way, certainly geographical proximity is not a sufficient condition for the development of cluster. So, what other factors might be responsible for the observed patterns? And is clustering a necessary condition for the development of biotechnology?

Recently, international trade theorists and industrial economists have re-discovered what urban and regional economists have long taken for granted about this issue (Breschi and Lissoni, 1999). For example, Henderson (1986) lists four sources of location externalities, three of which come directly from Marshall and can be found more or less unaltered in Krugman (1991):

a) Economies of intra-industry specialisation: a localised industry can support a greater number of specialised local suppliers of industry-specific intermediate inputs and services, thus obtaining a greater variety at a lower cost.

b) Labour market economies: a localised industry attracts and creates a pool of workers with similar skills, which benefits both the workers and their employers.

c) Ease of communication among firms: information about new technologies, goods and processes seem to flow more easily among agents located within the same area, thanks to social bonds that foster reciprocal trust and frequent face-to-face contacts. Therefore adoption, diffusion and innovation seem faster and more intense in geographical clusters than in scattered locations. That is, some "knowledge spillovers" exist, which are geographically bounded.

d) Public intermediate inputs: local authorities may place a stronger than usual effort in providing them as soon as they recognise the importance of a specific industry for the welfare of the local communities.

All these agglomeration forces can play a role in defining a cluster of innovation. Definitely, point a), b) and to a lesser extent d) played a role in the case of Lombardy. Thus, localised innovation advantages may arise even in the absence of agglomeration force *c)*. However, this is precisely the force that has attracted most the attention of most economists and fascinated many policy-makers, especially in the case of biotechnology and with specific reference to university – industry relationships.

The role of geographically bounded knowledge spillovers is linked to tacitness. Tacitness implies that personal contacts, imitation and frequent interactions are necessary tools for knowledge transmission, and ones which are clearly available at a lower costs for firms located within the same city or region (Swann and Prevezer, 1998). Regional economists have built upon such observation, and added many socio-economic features to the need for agglomeration. In particular, they have pointed out that the transmission of tacit knowledge requires mutual trust, a sharing of language and culture, as well intense non-business relations. Thus social networks, such as those one can find in areas with a homogenous social background, appear to be key carriers of tacit knowledge (Breschi and Lissoni, 1999).

However, very little is known about the precise ways by which knowledge is actually transferred among people located in the same geographic area. The usual story assumes that by being near to universities and other innovative firms, employees of local firms will hear of important discoveries first and thus be able to utilise them before others are aware of their existence (Zucker at el., 1998).

However, some authors (Zucker, Darby and Brewer (1994 and 1997) and Zucker, Darby and Armstrong (1998) have argued that the standard notion of geographically localised knowledge spillovers, according to which firms located nearby universities are most quickly exploiting commercially the results of basic research since they can most readily learn novel results thanks to the 'social' ties between employees and university scientists or to the possibility of attending informal seminars at the university, does not seem to apply to the case of biotechnology industry, at least in the phase of its emergence. Rather, they argue that discoveries in this technological area are characterised by high degrees of *natural excludability,* i.e. the *techniques* for their replication are not widely known and anyone wishing to build on new knowledge must gain access to the research team or laboratory setting having that know-how. In these circumstances, the discovering scientists ('superstars') tend to enter into contractual arrangements with existing firms (contract or ownership) or start their own firm in order to extract the supranormal returns from the fruits of their intellectual human capital. Moreover, the scientist work with or create a new firm within commuting distance of home or university (where they tend to retain affiliation) thus creating localised effects of university research.

These authors show that the innovative performance of biotechnology firms is positively associated to the *total* number of articles by local university 'star' scientists. However, when the number of articles written by university stars is broken down into those written in collaboration with firm scientists ('linked') and the remaining ('untied'), the coefficient on articles written by local university stars *not in collaboration* with the firm loses its significance and nearly vanishes in magnitude. Previous evidence on the existence of indiscriminate localised knowledge spillovers seems therefore to have resulted from a specification error, i.e. the inability to control for the actual relationships linking *individual scientists* to *individual firms*.

These results suggests some conjectures:

a) At least in the early phases of new industries, knowledge is not 'in the air', but is embodied in individual scientists and research teams. Social ties and personal contacts are not sufficient to gain access to naturally excludable knowledge. This requires deep involvement in the research process and bench-level scientific collaboration. If anything, this result tends to support the idea that one must invest resources not simply to *search for* new knowledge, but to build the competencies to *absorb* the knowledge developed by others and to understand the highly context-specific "codes" into which knowledge is translated.

b) Naturally excludable and rivalrous knowledge does not spill over, but people (teams) embodying knowledge move (locally) across organisations in order to exploit the value of their knowledge. In other terms, localised effects of university and industry research are most likely to result primarily from a combination of appropriability of tacit non-replicable knowledge and low geographical as well as organisational mobility of researchers.

It is also worth mentioning that the assumption that inventors and firms operating in a *specific industry* and in close spatial proximity to each other will be more innovative than those who are geographically isolated because of the greater likelihood that they will share (tacit) knowledge has been criticized by Lamoreaux and Sokoloff (1997). Summarizing, they show that:

i) Concentration of firms and production in a given area is not *per se* a necessary and sufficient condition to determine high rates of innovative activity. To put in slightly different terms, *static externalities* related to the current scale or size of an industry in a given city do not necessarily generate better (local) information flows to the advantage of innovative activities. What seems to matter more is the *accumulated* stock of knowledge (*dynamic externalities*) in a diversity of industries as well as the levels and types of human capital in a region. Regions that first emerge as centres of innovative activity in a certain industry tend to maintain their advantage over time.

ii) Industries may move across regional and national borders without a corresponding re-location of inventive activity. Inventive activity is more 'sticky' than production. Of course, it remains to be seen why it is so. On the one hand, there is the possibility that the locational stickiness of inventive activity derives from the reluctance or lack of incentives to migrate by people with knowledge and experience in an industry. On the other hand, a possible explanation could relate to the richness of *general technological know-how* in higher-order regions that serve as an effective substitute for specific knowledge and allows to find new applications across a wide range of industries.

iii) Institutions matter for regional innovation, but in a different way than frequently claimed by many regional economists. These latter tend to stress the role played by 'soft' institutions like trust, norms, codes of communication, conventions, in facilitating the process of information sharing among firms and individuals. According to another perspective, institutions are also important because they help to build those 'bridging' market mechanisms that mediate relations among inventors, suppliers of capital and those who are willing to commercially develop or exploit new technologies.

Finally, empirical evidence has been recently collected to show that linkages bounded by proximity are not always key to innovation (Echeverri-Carroll and Brennan, 1999). These results obtained show quite convincingly that *local* sources of knowledge are key in determining success in the development of new products and processes only in areas with a large accumulation of knowledge (e.g. Silicon Valley). On the contrary, innovations in firms located in cities with a relatively small accumulation of knowledge depend on the relationships with universities and other high-technology firms (suppliers and customers) located elsewhere, especially in higher-order urban centers. More specifically, the results of this study permit to draw a number of important conclusions:

a) Local boundaries play a fundamental role for the recruitment of skilled workforce and technical personnel. The presence of other firms working on similar or related things is important not only as a direct source of engineers and scientists, but also because of the indirect effect of reducing the likelihood that a skilled worker will suffer a long period of unemployment. In other words, local areas are important also for *non-knowledge related* agglomeration economies.
b) The most dynamic and innovative firms look for knowledge embodied in engineers and scientists wherever they are available, and not necessarily constrained in this by geographical barriers. The question on the importance of intellectual human capital (engineers and scientists) developed *within* the metropolitan area was given on average very low rates by fast innovators, whereas they scored very high the question on the availability of frequent flights connecting to other high-tech regions (i.e. Silicon Valley).
c) *Local* knowledge sources are relatively less important for firms located in lower-order regions. For these firms, local universities are viewed as suppliers of skilled workforce, rather than loci of innovations or sources of product ideas or spillover effects. In order to sustain high rates of innovation they must develop linkages with actors (universities and other high-tech firms) located in higher-order regions (see also Lyons, 1995)[12].

Trying to draw some conclusions from this discussion, it would appear that clustering may be the outcome of different factors, but mainly:

i) the existence of a strong critical mass of scientific knowledge, in absolute terms: in other words, excellence in scientific research is a basic precondition for attracting innovative activities. Absent this, firms (incumbents and/or prospective entrepreneurs) might look

[12] In a related vein, Suarez-Villa and Walrod (1997) have supported the idea that not locating in a spatial cluster may actually hold advantages, by allowing firms to safeguard their privacy and to introduce new products earlier than their competitors.

for other locations for tapping the relevant knowledge. Moreover, diversity is also important. Insofar as innovation rests on the integration of different fragments of knowledge, the presence of a diversified scientific base becomes a key issue.

ii) The existence of a strong and diversified industrial base, with accumulated capabilities and organizational structures enabling them to actually participate in the network of cognitive and social relationships that are necessary to get access to, to absorb, integrate the new knowledge and, on these bases, to engage in successful innovative activities.

iii) The existence of specific and often formal organizational devices (including markets for know-how) that allow flows of knowledge to take place.

6. Conclusion

In this paper, I have argued that the sluggishness of the development of biotechnology in Italy was due to the lack of most of the basic preconditions for the take-off of innovative activities in this field, as it concerns the scientific and industrial base, the organizational structures linking science to industry, venture capital and intellectual property rights.

Innovative activities clustered, but did not take off, in those regions, primarily Lombardy, where at least some of these preconditions were in part present: mainly as it concerns the availability of good science and a solid industrial base. Such conditions were however not sufficiently developed. As a consequence, biotechnology did not take off.

Finally, I have also argued that clustering is a likely, but certainly not a sufficient condition for the development of innovation in biotechnology and perhaps not even a necessary condition. A cluster may develop if all the above mentions pre-conditions are in place and if “hard” organizational devices for sustaining intense knowledge flows are created.

These observations might have some implications for policies. Indeed, in recent years European biotechnology seems to have found a new dynamism and even in Italy and in Lombardy some interesting developments are taking place.

One interpretation of this dynamism might be that policies might – at last - have begun to exert some impact. In many countries, measures have long been taken to introduce within Europe some (or parts of) of the typical American institutional features which have been crucial to the development of new biotechnology start-ups. Thus, policies have been targeted at fostering venture capital, at developing financial markets tailored for new high risk companies, at promoting the commercialization of academic research and the mobility between academia and commercial activities. This is certainly the case of Germany and perhaps of France, too. In other countries, however, the effect of policies seems to have been much smaller. And even in the German case, the effects of Bio Regio have been widely different across regions. This, in turn, may be the outcome of different policy designs and/or of other structural conditions. In general, it would seem to be the case that there are minimum critical thresholds that policies have to overcome before they can have some impact and that in any case interventions aimed at modifying institutions and deeply ingrained forms of behaviour take time.

So, changes in other structural conditions may have played an important role. A primary candidate is to be looked at in a general process of maturation and catching-up in the scientific, technological and organizational base of European biotechnology, mainly as it concerns basic research in universities and in large established companies. As it was argued in the paper, the strength and width of the knowledge base, both in universities and in industry, and its integration in efficient organizational forms, was and remains perhaps the single most important factor in explaining performance in biotechnology. Thus, the increasing diffusion of molecular biology in the general training of doctors and in the medical practice, an increased integration of research and teaching, the widening and the increasing integration of the research base in Europe produces now state-of-art knowledge that can be exploited by NBFs, at least in specific niches, and by large corporations which are now in the position to express a qualified demand for such research and services[13].

To be sure, the gap with the USA is far from being filled. Moreover, the institutional structure of most European countries remains profoundly different from the American one. Thus, the future of the new European NBFs and of the patterns of evolution of the biotechnology industry remain to be seen. However, some tentative implications might be drawn from this case.

First, policies can and do have effects, especially if they overcome some critical threshold and they are "integrated", i.e. they act simultaneously on all the relevant variables. Second,

[13] It could also be noted that the take-off of the European start-ups has been taking place in conjunction with the emergence of new technological trajectories based on generic techniques. Certainly in Germany, but not in Italy, most new start-ups are indeed active in these areas (Casper 1999). This may not have occurred purely by chance, because these techniques have characteristics that make them relatively easier to develop within the European technological and institutional environment. First, it is intriguing to think that these techniques represent in a way a sort of revenge of the old chemical-based research paradigm in pharmaceuticals. Their function is essentially to allow for the fast screening of thousands of potentially promising compounds, as it happened – at an infinitely lower speed – at the times of "random screening" before the molecular biology revolution in pharmaceutical research. To the extent that the "culture" of the European industry has remained more closely linked to the old paradigm, it should come as not too big a surprise that it is in these areas that new start-ups have more chances to be born and prosper. Second, the new companies embodying competencies in these fields are profoundly different in their nature from the other types of NBF. Precisely because they are based on generic, transversal techniques, their core competencies are less unstable and technical change is less competence destroying for them. Moreover, they can interact with a large variety of different agents and have in principle a much larger market. Similarly, lead times are much shorter, because sales are usually on a contract basis and immediate. As a consequence, their risk profile is also comparably lower and access to capital comparably easier (Casper 1999).

however, policies take time before exerting their effects. Third, the development of a strong research base and of strong technological competencies remains a crucial pre-condition for industrial dynamism and also for the efficacy of other policy initiatives aiming at inducing institutional and cultural changes: the creation of appropriate incentive mechanisms is clearly an important issue, but incentives without competencies may be totally ineffective or even dangerous.

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Table 1

Major biotechnology innovators in Italy

1978-1990

Institution	Number of EPO Patent*	% of total Italian patents*
Eniricerche	12	25.0
Sclavo	7	14.6
Farmitalia Carlo Erba	6	12.5
1990-96		
Eniricerche	16	14.7
Biocine	10	9.2
Pharmacia &AMP Upjohn	9	8.3
Consiglio Nazionale delle Ricerche	9	8.3

- Patent applications at the European Patent Office
- Source: EPO-CESPRI Data-base
