Institutional and financial requirements for the emergence of biotechnology in Brazil

Maria da Graça Derengowski Fonseca (IE UFRJ)♣

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♣ Associate Professor, Institute of Economics – Federal University of Rio de Janeiro -IE/UFRJ Rio de Janeiro derengow@ie.ufrj.br and mariagdfonseca@yahoo.com.br

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Abstract

It is widely recognized that Brazilian biotechnology activities suffered an explosive upraising during the second half of the nineties, demanding new institutional tools to spur local R&D, mostly 'in house' research. In spite of that, traditional sources of financing biotechnology are still inadequate, because it has merely focused on scientific sponsorship. The main reason is that the rise of venture capital in Brazil is still developing. Thus, the budget that would finance R&D activities is falling short. Furthermore, the rise of new companies depends on more efficient intellectual property right regulation and a clearer structure of enforcement. We believe that the lack of adequate intellectual property right legislation is an obstacle to universities spin-offs of start-up for biotechnology companies. The purpose of the paper is to analyse the institutional environment and the financial requirements for the development of biotechnology companies in Brazil. The paper also presents data from a preliminary survey of the biotechnology sector of the DPP FINEP research [2].

Key words: biotechnology, complexity, sectoral systems, institutional environment,venture capital and Brazilian start-ups.

1.Biotechnology as a complex adaptive system

The word *biotechnology* was invented in the finance sphere, more precisely in Wall Street, to designate a set of techniques and tools that can be used to produce useful products or to advance scientific experiments. Biotechnology has been defined as the intentional manipulation of living organisms, through a research-based program, in order to achieve a useful end product (O´Reily,1987; Gibbs & Kahan, 1986: Korwek, 1992). According the Biotechnology Industry Organization (BIO), biotechnology is a collection of technologies that capitalize on the attributes of cells, such as their manufacturing

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capabilities, and put biological molecules, such as DNA and proteins, to work for people (www.bio.org)[3]. The commonly used definitions of biotechnology are[4]:

1) *Classical biotechnology*: technologies that have been used for thousands of years for the production, mainly on the basis of experience;

2) *Modern Biotechnology*: the more science based development of the classical biotechnologies, a development which started in the 19th century;

3) *New biotechnology*: the technologies which developed from the late 1970s including genetic engineering and cell fusion.

Biotechnology can be been defined as a robust block of scientific knowledge, institutions and technological information, which combines already existing research protocols and methodologies with new scientific concepts derived from distinct disciplines such as molecular biology, genetics, *proteomics*, functional *genomics*, and biochemistry. This definition holds a great potential for new combination and interaction with other technologies activities and academic disciplines such as the ones representing computer science and information technologies (Fonseca, 2000)[5].

University researchers have been also forging relationships with the pharmaceutical industry and the agriculture sector. As a consequence, new forms of organization hold up a complicated network of laboratories and R&D institutions with a multitude of medium and small-specialized firms. On the other side, the world's pharmaceutical companies are increasingly looking for innovation. They are, in many ways, becoming biotechnology companies themselves, integrating genomics into their R&D efforts and forging relationships with the university Together, they represent a complex but dynamic amalgamation of expertise, knowledge capabilities and proficiency[6].

These definitions could also be associated with the *sectoral systems of innovation* approach (SSI), which aims to provide a multidimensional, integrated and dynamic view of innovation in sectors (Malerba,2002)[7]. The SSI put emphasis on three dimensions of the process of innovation that affect the generation and adoption of biotechnology. They are: knowledge, networks and institutions. An innovation system is composed by actors or agents, the set of relationships among agents (the networks) and other contextual features which affect the decision process, like the development of knowledge and economic competences (Edquist and MacKelvey,2000).

[3] Man and woman have been using biological processes of microorganisms for 6,000 years to make food products, such as bread and cheese. In this paper we understand biotechnology as the use of cellular and bio-molecular processes to solve problems or make products.
[4] This definition is inspired in the OECD (1989) classifications from 1989 with few modifications.
[5] The so called *molecular biology building block* combines molecular approaches with rDNA technologies, proteomics, genomics and bioinformatics (Fonseca,Silveira and Dal Poz,2003).
[6] According to Teitelman(1989) biotechnology is, at its heart, a *bureaucratic science:* an attempt to organize and rationalize serendipity. This romantic definition is closer to Kuhn ´s definition of *normal science.*
[7]See Malerba (2002) and also MacKelvey et al. (2002).

As a consequence, the knowledge approach could be integrated to the genetic information-based complex system characterizes a *particular combination* of scientific knowledge and technological procedures adopted by groups of researchers and scientists aggregated in research networks (Fonseca et al., 1999). The biotechnology stock of knowledge does not cease to develop new specific, tangible and intangible, assets. Furthermore, the strategies and the rules played by the main actors of the innovation processes – including the entrepreneur and the capitalist- are constantly being puzzled by those flux of information.

On the other hand, the P&D efforts are usually understood as *guided by technological empiricism*, resorting to science only when they face impediments in the innovative processes. One of the main difficulties of dealing with biotechnology is that despite the immediate recognition of new opportunities, the economic basis of biotech products and markets have not been completely established - neither the payoff, nor the rules of the game played by firms and other agents[8].

When a new biotech research program is designed, both scientific and technical decisions must be anticipated, regarding not only the economic impacts but the feedbacks created from technical problems and regulatory framework. These problems could easily define a technological trajectory. This is the case of the vaccine's flaws or allergies caused by inappropriate use of gene sequences in transgenic experiments. Nevertheless, new scientific disciplines are constantly imposing new scientific routes and new directions for biotechnological change. It does not mean that biotechnology has no technological drive. Actually, both technological routines and scientific procedures must be taken in consideration when firms are truing to anticipate profits. Furthermore, they could also be taken as targets or *guide-post* (Sahal, 1985) for those companies and organizations engaged in R&D biotech projects[9].

However, there are different forms of integrating biotechnology to industries and sectors. Supporting to the main achievements of biotech advances in human health one can situate pharmaceutics capability of escalating financial funds and sustain the commercialisation of biotech products. One can also call attention to the compliance of consumers to take risks related to new biotech drugs. In straight opposition to what happens in the pharmaceutical industry, the industrial structure associated to the agricultural products is less concentrated. Agriculture displays interests that not always converge to the same objectives. Biotechnology for agriculture is connected to a vast set of activities that range from agriculture trough big business, from the transformation of raw agricultural material organisms into products and services.

Concerning the applications of the biotech research, advantages in human health are lined up almost symmetrically with difficulties in agriculture. After that a huge problem for

[8] The emergence of biotechnology innovations presents new conceptual challenges, once biotechnology processes do not necessarily follow the classic Schumpeterian *discovery-innovation-adoption* sequence

[9] The.GENOMA Program is a very good example of that peculiar combination of science and technology matrix offering simultaneously the technological route and the economic target for entrepreneurs engaged in the genome hunting race. However, the GENOMA has opened de box of Pandora of technological opportunities "blowign up" the set of previous recombinant DNAchoices (Fonseca, Silveira and Dal Poz,2003)

the development of the vegetal biotechnology refers to its problematic regulation and definition of the standards for research activities practices. The perspective of obtaining profits in therapeutic medical research is considered good and the benefits of introducing successful products are extremely high. According to Casper and Kettler (2000) the leading selling therapeutic product can raise in billions of dollars the profit (per year) of a patent. However, the time period expected for biotechnology *"revolutionise healthcare*" through treatments tailor-made to the disease can last for over a decade.

2.Searching for Funds: a glimpse of biotech markets

Eighteen years ago, Craig Venture worked for U.A. governmental laboratories before he had obtained the capital to apply in his own biotechnology business. At that time he had to beg for grants as any other microbiologist in the world. On February 2000, his firm raised $ 1 billion in only one day on the New York Stock Exchange (The Guardian, 6/05/2000). Since then, Venture – and Celera- has been turned in the model of a successful innovator entrepreneur in the biotechnology business. Venture proceedings are nevertheless founded in very risky strategies[10].

Biotechnology is progressively becoming a market reality. However, biotechnology competition does not show a completely structured pattern like other high-tech industries. Biotech sales and revenues are not directly linked to final demand and are still depend upon the rate of scientific and technological activities that public and private sector have been carrying in the last ten years. Consequently revenues are strongly dependent to governmental the repertoires of governmental policies.

Biotechnology drugs, vaccines and diagnostics are now part of medical mainstream. After three decades, biotech pharmaceutical companies have brought to light more than 155 innovations, drugs, vaccines and diagnostics approved by the FDA, the main regulator body in U.S, helping more than 350 million people worldwide[11]. Regarding at the pharmaceutical sector, one can say that the potential of biotechnology could be summarized by the fact that biotech pharmaceutical comprises 5% of the industry total sales and 25% of new therapeutic entities.

More than 370 biotech drug products and vaccines are currently in clinical trials in the United States targeting more than 200 diseases, including different kinds of diseases like cancer, Alzheimer, heart disease, diabetes, multiple sclerosis, AIDS and arthritis. Biotechnology is also responsible for more than hundred of medical diagnostic tests developments, keeping the blood supply safe from virus, making home pregnancy tests and helping to detect other illness.

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[10] Celera Genomics is actively engaged in basic and applied research and development programs designed to develop new therapeutic products. Celera has developed collaboration with large pharmaceutical companies and internal programs for discovering therapeutics for inflammatory diseases, including asthma, osteoporosis and rheumatoid arthritis for a long time and the genomic branch of this company has internal programs for discovering therapeutics for the treatment of thrombosis and various types of cancer, including pancreatic and lung cancer. The firm is also improving its capabilities in proteomics, bioinformatics and genomics in order to identify and validate drug targets and diagnostic marker candidates and to discover novel therapeutic candidates. Celera Discovery System online platform is an integrated source of information based on the human genome and other biological and medical source.

[11] According BIO seventy per cent were approved in the last six years.

United States have dominated biotech pharmaceutical business, accounting for 73% of revenue and more than 74% ($16,3 billion) of research and development spending in 2002 and near 74% of employees 2002 (Table1). Europe biotech industry represents 20% of global revenue and 23% of global R&D investments[12] creating 1,9 million jobs (43%).

Table 1 - Global Health Biotechnology in 2002- Public Company Data

	Global	U.S.	Europe	Canada	Asia
Revenue*	41,369	30,266	8,262	1,473	1,375
R&D Expenses*	22,012	16,272	4,989	0,555	0,197
Net Loss*	12,483	9,378	2,763	0,263	0,079
Employees**	193,76	142,9	33,304	7,785	9,764
No of Companies	4362	1466	1878	417	601
No. Public Companies	613	318	102	85	108
No. Private Companies	3749	1148	1776	332	493

Source : Ernest & Young

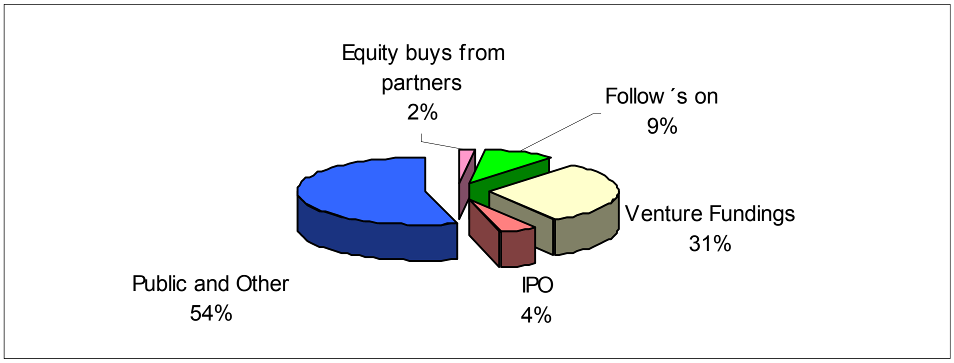
Source: BIO based on Ernst & Young LLP, annual biotechnology industry reports, collected in2001/02[13].
Number may appear inconsistent because of rounding

According to Ernest&Young (2003), biotech U.S. revenues increased from $8 billion, in 1992, to more than $ 28 billion, in 2001. The five biotech leaders, Genentech, Amgen, Biogen, Chiron and Genzyme shared 33% of total U.S. biotech revenues spending an average of $133,600 per employee on R&D in that year. All these countries have been experimented net losses of 30% on average in relation to revenue.

Raising funds in the stock market is the faster way of obtaining money in the U.S. On the other hand it is a very risky activity and only a small fraction of thousands of potential drugs is well succeeded, subsequent to hazardous process of clinical trials and regulatory approval.

[12] The total value traded by 318 biotech public companies in the United States rose from US$45 billion in 1994 to US$206 billion (at market prices).Biotechnology Industry Statistics BIO, 2003.

Figure1- U.S Biotech Industry Financing



Millions of dollars

In point of fact, few shares are as so speculative as biotechnology shares. The main reason for that is uncertainty related to innovation and regulation issues. The so-called "would-be" biotech drugs might fail in clinical trials or products and services that could be refused by regulators, like GMO´sproducts. But there is another more technical explanation. According SG Cowen, a New York associate to Societé General Bank, biotechnology *fundamentals* does not really count (Economist 25/03/1999). Fund managers are main responsible for the biotech boom driven by bonuses that depends less on absolute performance of these funds and more on their relative position. In those circumstances, buying volatile shares looked like… *a one way bet*[14]. Venture capital has represented the typical form of funding biotechnology.

The outcome is widely distributed along the financial chain, from the venture capital funds to individual private agents who supply *seed money* to convert promising ideas in business plans, the so called *angels*. The incentives for fund managers and venture capitalists are different. However, they take advantages of stocks to shorten losses creating a feedback in the opposite directions[15]. In the absence of flotation, ventures capitalists had not option but stay in the market carrying the losses of selling at low prices estimated assets to pharmaceutical big companies. Consequently, the *speculative* business results in investments opportunities.

At the moment, biotechnology investors in developed countries are long run forecasters looking forward very profitable future markets and new opportunities to substitute traditional - possibly banned by environmental regulations - products, like pesticides or antibiotics. Long run expectations on the future revenues generated by profits from the sales of new products, services and equipment have to sustain the continuous flow of investments, financed by different forms of funds, including stock exchange. Unlike the investment discontinue which affected the majority of high tech sectors, the explosion of NASDAQ bubbles in 2000 set aside a substantial percentage of flow of biotechnology financial funds in the U.S. (Economist 01/04/1999).

[14] If the shares drop, a share holder will be little worse than if he or she had bought something safe.

[15] This is what economists call a *self-fulfilling prophecy*.

The bubble was generous with biotech companies but big biotech business is doing better since the mid nineties[16]. Biotechnology corporation, with market capitalization of $1 billion or more, had a grow of 7% in the value of their shares since the beginning of 1999, but small firms, with market capitalization less than $200m, have fallen in value by 12%, (Hambrecht and Quist, 2003 and Fortune 2003). Such gaps between big and small firms are common in many industries. However, they are particularly disturbing in the biotechnology industry, where 4/5 of companies have market values of less than $250m (Economist 25/03/1999).

Venture capital investments play a very important role during the establishment and early stages of new biotechnology firms. Although investors must have easy exit choices even before they agree to make business with biotech companies (Casper&Kettler,2000). According to MakKelvey et al.(2002) venture capital was a long standing institution in the North American financial and innovative systems. It was already active since 1920 and emerged as a vibrant industry with the electronic revolution in the 1960´s. Arthur Andersen (1997) had estimated that over the turn on and early development phases alone that each company needs somewhere between £2-12 million depending on their product focus. Normally the new start-up companies are interested to improve their research tools not with the purpose of become a typical drug producer, but *providers of services* to the pharmaceuticals corporations. In the case of developing biotech therapeutic products, however, reserving enough money for the clinical development is absolutely important. The cost of developing a new drug can be estimated between $100 and $200 million (Casper&Keppler, 2000).

In the start-up phase funds can be obtained from the business angels, internal resources, venture capitalists, large pharmaceutical companies or other financial sources. Venture high risk capital is hard to sustain in countries without large capital markets willing to support high risks initial public offering. This issue explains the leadership of U.S. and the U.K. Just about all U.S. biotech companies were funded by venture capitalists. The reason is that financial markets essentially support the property rights structure of incentives, especially capital market for technology firms like NASDAQ (Casper & Ketller, 2000). As emphasised by these authors (2000:8):

> *Most importantly through the NASDAQ exchange, massive capital market exists in which thousand technology firms have successfully taken listings. While these markets have a strong "short-term" orientation, several hundred loss-making firms, or products going through clinical trials have successfully maintained listing within US stock exchange – and in many cases used strong stock market valuations to leverage continued expansion of firms activities.*

The success of biotechnology business in the United States cannot be solely explained by private funds. The United States Institute of National of Health has doubled over the past five year to $23 billion for basic research (Fortune,2003).More than 40 states in the U.S. have been developing aggressive biotech development programs to help star-up companies in the transaction of biotech products and services

[16] This is one of the explanations for the net losses in Table 1.

There are important differences in the way biotechnology is financed and organised in Europe. Those differences are mainly related to the degree of control that financing agencies have on research activities, that is, on *ex-ante* valuation activities than on the potential of the research (Assouline e Joly, 1999). Despite the standard view of associating European countries with a greater degree of intervention of the state, there are considerable differences between different countries under study. British biotechnology leadership in Europe is a fact. Nearly two thirds of the commercial revenues of European biotech are represented in the U.K. biotech sector. This country is still the European leader in terms of total number of companies if one considers that public companies were scheduled on stock markets. U.K. also has a variety of mature firms, consequently presenting high employment figures (McMeekin &Tampubolon, 2000).

The biotech market in Germany has exploded in the nineties, with 50 to 60 new companies being created annually. The number of entrepreneurial life science companies grew from 279 in 1999 to 358 in 2000. Merger and acquisition in German pharmaceutical industry has also been also eloquent. However, mergers in German biotechnology have not been considered as important as co-operative alliances between companies to pursue common goals rather than movement toward acquisitions. Venture capital was scarce in Germany until the late of the 1990, presently, 21 biotech companies are publicly listed on *Neuer Markt*, with a market capitalisation of 9,77 billion Euros (Ernest Young, 2001).

Between 1998 and 2000, E$3,5 billion in venture capital funds were available to biotech companies in Germany (66% in 2000)[17]. Money raised by biotech companies at initial public offering ranges from a low of approximately E$30 (e.g., Rhein Biotech, Morphosys) to as high as E$120 million (e.g, GPC Biotech, Medigene). Despite unprecedented levels of private financing obtained by German biotech business in the last years, many companies continue to receive a significant portion of their funding from the government and about DM1,5 billion years from the German Ministry for Education and Research are supposed to be allocated in biotechnology in the next five years.

[17] The largest source of this funding is MPM BioVentures, a division of MPM Capital that invests exclusively in biotechnology. MPM Capital has investment resources totaling 600 million euros. Other important VC investment firms are Apax, Atlas Venture, 3i Group, Deutsche Venture Capital Gesellschaft (DVCG), Earlybird, LifeScience Ventures, Techno Venture Management (TVM), and several more regionally focused funds.

3.Do institutions make a difference?

According to MacKelvey, Orsenigo and Pammoli (2002) biotech start-up integrate the core of the new biotechnology pharmaceutical competences making innovation critically dependent on publicly generated scientific research generated into the universities. In many countries, the appearance of biotechnology start-up represented a genuine new competitive force in the pharmaceutical industry. At the beginning, they were primarily university spin-offs formed through collaboration between scientists and professional managers, backed by venture capitalists.

The first biotechnology company, Genentech, was founded by Herbert Boyer, one of the creators of recombinant DNA - the science of genetic engineering that started the biotech industry - and Robert Swanson, a venture capitalist. It is now the world largest biotechnology company. Amgen, a start-up in 1980, attained its status on the strength of two drugs, Epogen and Neupogen that have annual sales in excess of $1 billion (Fortune, 2003) [18].Amgen and Genentech have achieved rival status with traditional pharmaceutical companies.

The first generation of biotech start-up have developed the scientific knowledge to understand the processes involved by protein and to identify the specific therapeutic effects of such produce protein (MacKelvey,1996). The first biotechnology product, human insuline, was only approved in 1982 however over 100 biotech drugs were in clinical development in 1991(21 were submitted to the FDA). From 1982 to 1992, 16 biotech drugs were approved in the United States. But only three products showed significant commercial success: insulin from Genentech &Lilly, tPA (1987) from Amgen & Ortho and erythropoietin (1989) from Genentech (Grabowski and Vernon,1994 and MacKelvey, Orsenigo and Pammoli,2002).. For that reason an health care investment company in New York said that “a biotech company is a pharmaceutical company without sales” (Economist March 20th,2003).

The firs generation of start-up firms were apt to mobilize specialized knowledge created in the universities and to transform it in potentially commercially useful techniques and products. However, with the exceptions of Amgen and Genentech, they had not developed the necessary experience and expertise to act in clinical tests and marketing, a necessary condition to be admitted into the selected environment of the pharmaceutical industry (MacKelvey,1996). For that reason they acted as research companies and specialised supplier of high technology intermediate services. At the beginning of the 80´s, these biotech firms had developed specific long term contracts to perform research services and supply specialized intermediate products in collaboration with pharmaceutical companies. These contracts were basically designed to protect scientific and technological secrecy and intellectual property rights of R&D.

Twenty years latter, new forms of scientific collaboration have opened new opportunities for biotech start-up firms paving the way for subsequent grow. From the university laboratories to small specialised niches and, then, to pharmaceutical sector, these

[18] Epogen is a red blood cell booster for anemia and Neupogen a white blood cell booster for reducing risks of infections.

biotech companies grew up as never before. At the same time, the networks of collaborative relationships among university and firms have also increased to unimaginable proportions. Later generations of start-up companies, like Incite and Celera, were largely created on the basis of scientific specialisation in DNA engineering, genomics and proteomics. They are also using the so-called "platform technologies". In some cases they are able to sell specialised services to a wider range of potential buyers, generally other companies or laboratories. On the other hand they are prepared to establish collaboration with larger incumbent pharmaceuticals companies and, in few cases, to merger with big pharmaceutical companies.

The success obtained by biotech firms can also be explained by the different institutional frameworks that have been established in different economic situations. Those frameworks could generate distinctive strategies and organisational capabilities at the sectoral level (Casper and Whitley,2002). Coordinated economic markets, like Germany and Sweden, could develop strong institutional framework to govern those collaborative forms amongst companies, universities and public funds. Coordinated market economies typically display quite high levels of non market through credit based financing, strong business association and state supported technical standards settings and technical development.

Liberal market economies, such as U.S. and U.K., shows a more flexible form of institutional arrangements *that are conducive to the development of project based entrepreneurial technology start-ups focusing on the discontinuity of radical innovation.* In contrast to that pattern, liberal market economies are based on market-based forms of industry coordination, generally supported by (more or less) government regulations. Typical institutions include marked based funding and patterns of corporate governance decisions (*ibidem*). In market economies, venture capital performs a crucial role of putting individual agents – researchers and angels- together. It also develops the crucial role within the new innovation of bio-pharmaceutics and innovations for agriculture.

According to MackKelvey (2002) venture capital provides first of all finance to prospective academic entrepreneurs. In this function, venture capital is not only advancing finance, contributing to strengthen the start-ups firms, but also provides managerial advice and organisational capabilities. In this function, venture capitalists help to bridge science to markets. Doing that, they also need to develop their knowledge about science and technology. Thus a significant number of PHDs from Academia end up working in venture capitalists firms. Consequently venture offers the cement to mix technology academia and finance (about this interesting point of view, see Teittelman, 1989).

4. Brazilian Biotechnology Institutions: an empirical approach

The high level of risk and uncertainty associated to research and development results in biotechnology fields are more easily tracked when private investors are supported by institutional networks and public organizations, not only by public funds. This is particularly true in the case of countries like Brazil, with some tradition on scientific and applied research in areas comprising building blocks we had mentioned above, like breeding techniques, biochemistry, immunology, bio-physics, bioengineering, evolutionary genetics and more recently, bio-informatics. Therefore, about 80% of the total biotechnology investment in the country is done by Brazilian governmental research institutions and universities - where 90% of the properly qualified labour is found (Silveira, Fonseca *et alli*, 2003). It is easy to deduce that, in Brazil, biotechnology development has been treated by a "technology push" point of view, neglecting demand side issues.

Recently, investments programs in R&D through government autarchies and state-owned companies have been trying to incentive formal and informal relationship with few emerging small companies. It is also easier to find alliances between "key biotechnology public organizations (Silveira, Fonseca and Dal Poz, 2003) and multinational biotechnology divisions (life sciences and human health) than partnership involving small and large firms in Brazil. The social-democracy period was marked by the effort to create public funds sponsored by fiscal exemptions and part of remittances to matrix of multinational companies (due to the payment of services and royalties), named "Fundo Verde Amarelo" managed by many committees composed by sector representatives.

The need of public funds to sustain Brazilian biotechnology is extensive to biotech public health companies. Immunobiological important producers, mostly vaccines and human blood factor, also depend on Brazilian governmental funds to raise money trough the National Immunization Program. This is the case of Biomanghinhos, linked to Fundação Oswaldo Cruz, Butantã and TECPAR

However, basic research and the investment in human resources are still strongly dependent on public funds, in the form of scholarships, equipment's and other laboratory facilities, entangling other sources of risk and uncertainty. It causes an unavoidable degradation of facilities in many research centres, coming from cut Ministry of Science and Technology's budget (MCT) off, for macroeconomic reasons (IMF agreement). Regular activities and investments in human resources are also affected negatively by these cuts. Brazilian universities are of great help in this issue.

They have been raising human capital, releasing scientific research and offering services to the population. Universities have also been offering adequate space to incubators in Brazilian science fields. Partnerships and contractual arrangements have been very important to small emergent companies in Brazil, spin off from public universities. During the nineties, Programs like RHAE (human resources training and formation program), managed by MCT, are very successful in transfer part of graduate students tasks to technology based firms in biotechnology, creating a profitable symbiosis between University and small enterprises.

In fact, there is a crescent number of spin off from universities in biotechnology, (Júdice, 2003). Actually, as in other countries, Brazilian founders of biotech new companies are also researchers from Brazilian main universities as USP- Universidade de São Paulo, Rio Grande do Sul and Campinas. We can mention many cases, like Extracta, a company linked to researchers from the Federal University of Rio de Janeiro, UFRJ.; Allelyx and Canaviallis, from Unicamp and UFSCAR; FK & Simbios, from UFRGS, Center of Biotechnology and ULBRA, in Rio Grande do Sul; RD Biotech, from USP-

Ribeirão Preto, São Paulo and BIOMM, from Biobrás and UFMG; and Hereditas, form CENARGEN/EMBRAPA-PUC-Brasilia- UNB, in Brasilia.

Among private companies, however few companies should be mentioned due to its large number of partnerships firmed with universities and other public institutions. This is the case of Valleé (5% of its annual revenue in R&D). This company has established an average of 6 research partnerships with universities per year to attain the internal development of the products. Table 2 below displays some other partnerships between public institutions, universities and private companies. The scope of the partnership is specified and takes from the production of pharmaceutical products trough the production of vaccines and researches in the biotechnological area.

Table 2 - Strategic partnerships between companies and key-organizations

Partneship	Resume
Bio - Manguinhos e Glaxo SmithKline	Vaccine *Haemophilus influenzaeB* (Hib), to be conluded in
Instituto Butantã e Aventis	Vaccine *Influenza*,
Instituto Butantã, USP e Sadia	Veterinary drugs.
Instituto Butantã - CAT , Biosintética, Biolab-União Química e Vallée	Veterinary drugs and vaccins.
Instituto Butantã - CAT e *Centre de Enérgie Atomique*, da França	Research on Molecular Proteins.
Instituto Butantã - CAT e Universidade do Japão	Drugs
Butantã e Tecpar	Human Vaccine (vacina tríplice)
TEcpar e Bio Manguinhos	Influenza Vaccine
Far Manguinhos/Fiocruz e Cristália	Drugs: Ritonavir , Saquinavir, Ritonavir + Saquinavir
Far Manguinhos/Fiocruz e Roche	Drugs: Benzonidazol
Far Manguinhos/Fiocruz e Médicos sem fronteiras	Drugs.
Far Manguinhos/Fiocruz e Glaxo Smithkline	Drugs: Abacavir, Amprenavir, Fosamprenavir
Far Manguinhos/Fiocruz e OMS	Drugs Megazol
Biobrás, UFRJ, Instituto Biológico - SP, Instituto Pasteur - SP, UFSC e Vallée	Veterinary drugs
Embrapa e Vallée	Clostridium control and Vet. Drugs Somatrofinaste
Universidade de Viçosa, Embrapa e Vallée	Biological pesticide
IAC e COPERSUCAR	New sugarcane varieties

Source: MCT (2001) by Silveira, Dal Pozz and Fonseca(2001)

To sum up, the need of alliances between public institutions, big companies and small entrepreneurs can be explained on the necessity to diminish the risks associated to such ventures that would limit the participation of private initiative. Since the late nineties, GENOMA programs in Brazil become another source of incentive to biotech activities. This program gives an relevant example of the above mentioned guide-post to a very large set of viable scientific and technology activities, gathering together universities, public laboratories (like LUZ-SINCROTON) and small technology based firms

The Genome Xylella is a symbol of Brazilian capability in developing leading research of a citrus pathogen that have been causing significant economical losses for economic activities in agribusiness activities in the state of São Paulo. The Brazilian Genoma is now being developed in more than 20 branches joining actors and institutions of multiple natures and reaching national and international levels of scientific relationship and technological importance. The networks that operate Brazilian Genoma activities in Brazil comprise specific researches on organisms responsible for production losses, such as the cocoa's tree parasite *vassoura de bruxa*, grapes, the citrus' pathogenic bacteria and the varieties of sugar cane and eucalyptus pulp amongst others.Besides, other initiatives in the field of human health involve Human Genome and Cancer Genome.

Based on a seed initial support of US$ 12 million (FAPESP, SP) and a follow-up fund of US$ 30 million, Genoma and its derivatives characterize a technology led policy, focused on the mobilization on different kinds of scientific and technological capabilities accumulated by public policies in the last 30 years.

Brazilian pharmaceutical market is amongst the ten biggest of the world. However Brazilian private funds invested in R&D for pharmaceuticals and medicine drugs are quite small. Consequently, the country internal market for these products is basically supplied by large multinational laboratories. Until 1990, Brazil was almost self-sufficient in terms of pharmaceuticals. As a consequence of liberalization of the Brazilian economy, in the 1990´s, branches of multinational laboratories reduced sharply research activities or specialization policies in the country, increasing the purchase of main ingredients and even formulate final medicines from their matrix. Since then imports of inputs and pharmaceutical drugs from other countries increased extraordinary. The international trend of mergers has also affected the industry in Brazil during the 1990´s. Biobras, the Brazilian producer of biotech insulin, was taken-over by Novo.

The Fundação Oswaldo Cruz – BioManguinhos plant - is the Brazilian leader in producing vaccines against measles, polio, meningitis A and C, and yellow fever. develops and produces reagent vaccines and raw materials for public health. It also has an appreciable production of substances for diagnoses (23 types of kits). The success of the efforts towards immunobiomolecules self-sufficiency is the outcome years of national stimulus to the domestic production. The autonomy can also be measured in terms of economy in public funds through the National Immunization Program (NIP). The latter reduced the occurrence of several diseases like mumpis, poliomyelitis measles. In some cases the economy of current public resources is huge[19]. Bio-Manguinhos is oriented for the production of diagnostic substances *in vitro* and *in vivo* and biological products. Both cases involve research on the intense use of recombinant DNA techniques, especially the production of recombinant antigens, the conservation of which is cheaper and use on humans is safer. In the molecular biology area, vaccines against *flavovirus* and others are being developed.

[19] According to the director of Butantã Foundation, the price of Hepatitis Vaccines imported from other countries declined from U$D 24 per dose to U$D 0.33 per dose in 10 years. See Silveira (org), Fonseca and Dal Poz(2002)

The Brazilian division of Ludwig Institute (ILPC), in São Paulo, is involved in the production and sale of biotech methodologies and procedures used against human cancer. The ILPC main projects developed are: Human Cancer Genome, with 1 million bases deposited in the GenBank, Bioinformatic Laboratory, the Genoma Center for clinical tests with diagnostic kits (genetic diagnoses of cancer), development of DNA micro-array biotechnologies, genomic of *papillomavirus*, and research on *prions*. The institute owns patents in the area of diagnosis - involving genetic expression tests based on mutations, and tests for analyzing proteins - as well as in therapeutics, namely, drugs for cancer treatment in copies of DNA *plasmids*. The ILPC also leads the *Xylella* Genome Project, launching the succession of sequencing GENOMA in Brazil

The competitiveness of agriculture is directly connected to the country ability to incorporate traditional biotechnologies in products and processes. Brazil is considered an *International Agriculture Research Country, i.e.,* a leader among developing countries besides India and Mexico (see Traxler, 2000). Distinctively to Mexico and India, Brazil relies on an extra advantage: its own financial institutional apparatus and budgets that are not dependent on international institutions like the *International Agricultural Research Centers* supported by FAO and other multilateral organizations.

Table 3, shows the features and relative different role of four organizations in vegetal biotechnology in Brazil, since a large public autarchy to a small spin off from UNICAMP, a Pro-clone enterprise. It is amazing to see the number of explicit and implicit contracts a small firm has be stabilising to face the challenges of a very restricted market.

The production of *commodities* and agribusiness products was affected positively by the traditional genetic research developed in key- public research institutions and companies. EMBRAPA was founded in 1971 to develop farming techniques, carries out research and encourage Brazilian agribusiness companies to adopt improvements and innovations. This company is also responsible for the positive results achieved by using conventional techniques for genetic improvement, especially in soybean production. The highly successfully introduction of soybean in the mid-west of Brazil (cerrado) during the 1970´s and 1980´s is a good example of Embrapa´s best research skills.

The governmental company are responsible for the use of *biobalistic* techniques, applied on pest control research, on amino acid food enrichment and on embryo transfer. Recently, Cenargem, the biotech branch of Embrapa has been developing important capabilities in the use of biotechnology for determining the variety of Brazilian natural resources, genomic analysis and comparison of genotypes of native wood by satellite. Cenargem also maintains the leadership in the development of recombinant technologies and genetic markers and is also in charge of the development of transgenic potatoes, beans and a new variety of papaya which is resistant to the *mancha anelar* virus. CENARGEN is also responsible for embryo transplant and bulk of embryos that are sources of germoplasm for future improvements in Brazilian livestock production (Fonseca *et alii,* 1999; Silveira, Fonseca & Dal Poz, 2003*).*

Table 3 -Synthesis of the Public and Private Institutions Operating in Biotechnology for agriculture in Brazil

Features		Public Institutions and Firms			
Dimensions	**Components**	**EMBRAPA (autarchy)**	**IAC (Public- recently APTA)**	**C.Biotec RGS (science- park)**	**Pró-Clone (private)**
Innovation	Position	Leader and follower at first degree.	Follower at first and second degree; Localized leadership in some areas, like cotton or horticultural crops.	Follower at first and second degree. Localized leadership in some areas, like animal health and inoculants	Follower at second hand; Market niche leadership- flowers matrices and potato seeds.
Management of purposes	1. Technology Vector 2. Novelty	1. Multiple and independent sources; 2. Radical and Incremental. Near by the Tech. Frontier.	1. Multiple and independent sources; 2. Incremental and less frequently, radical.	1. Multiple and independent sources; 2. Incremental and less frequently, radical;	1. Singular and Very dependent in sources of technology; 2. up-to-date intermediate biotechnology (micro-propagation. tissue culture)
Sources of Technology	Internal/ External	Both sources (tech. contracts).	Both sources.	Both sources, but biotechnology oriented.	External only; Local Scaling-up developments
Investments	1. Intensity 2. Size 3.Guidance 4. Approach	1. Above average 2. Larger than average 3. Basic and Applied 4. Covers the whole spectrum: from distinguished to mature technologies.	1. Average 2. larger than average 3. basic and applied 4. Covers the whole spectrum: from distinguished to mature technologies.	1. Below Average 2. Below average 3. basic and applied 4. Very specialized approaches, but using basic biotechnology tools.	1. About 10% of total income. Above average in the same class of biotech firms; 2. small size (US$ 150 mil/year); 3. Applied only. 4. Product Innovation. Mature technologies
Organizational Mechanisms	1. Formal Management 2. Relational Capacity 3. Control 4. Frame 5.Tech. Transfer	1. Emergent; 2. Wide and expanding; 3. Formal and Informal 4. Decentralized 5. Intense in both ways.	1. Looking forward to be market oriented; 2. Narrow and 3. Informal. Towards a more formal contracting activities. 4. By function. (genetics, microbiology, etc) 5.Informal means.	1. n.a. 2. Average, but market oriented by local firms 3. Small framework: based on academic hierarchy; 4. By function in biotech.	1. The owner is the leader; 2. High in comparison with similar firms. Agreements with Worldwide leaders; 3. Contracts 4. Centralized 5. Cooperation agreements with national and international firms.

Source: See also Solleiro and Castagnone (1999), *apud* Silveira, Dal Pozs and Fonseca (2001).

Embrapa network of laboratories maintain a significant number of contracts and agreements with large private companies including Aracruz, a *pulp and paper* Company and Monsanto. These contracts have helped to boost the development of knowledge and technical procedures for genetic and also for genomics in Brazil. They have also been decisive in the formation of networks for research and development of recombinant DNA techniques in Brazil. At least, people working in the laboratories of Cenargem have created two of the most efficient small biotech firms in Brazil. Besides, Embrapa also maintains several longer-term agreements with municipal authorities and association's states and farmers to develop and sustain corn enrichment programs to deliver to school lunch programs.

In the research frontline there are also a number of private projects financed by co-operatives like COOPERSUCAR, the main Brazilian association of the sugar producers in the State of São Paulo, and COODETEC a grain co-operative from the South of Brazil. The former has a partnership with UNICAMP in the Genoma Project (called *Sugar Cane EST* - SUCEST) a project focused on the sugar cane gene sequencing. In this research more than 80.000 genes were already identified, including the ones responsible for the resistance of the plants to heat and those that determine a better adaptation to different soil types. According Silveira, Fonseca and Dal Poz (2003) this is one of the biggest projects ever made to evaluate expressed genes in plants in Brazil. As other branches of GENOMA in Brazil, COOPERSUCAR supports agreements with the Texas University for the make up of DNA mapping and molecular studies of virus and parasites in sugar cane. There is also an agreement the University of South Carolina to develop DNA libraries and to improve résistance plants against specific disease as *rust*.

5. Biotechnology Start-Ups Companies in Brazil: preliminary results

There is currently few studies that evaluate the competitive data on biothech companies in Brazil (NBCs). This section uses some statistical developments present in the research for the Ministry of Science and Technology (MCT)[20]. It also drives some conclusions from Fonseca *et al.* (1999), prepared for PADCT/FINEP/MCT. However new information about competitive patterns, strategies and commercialization of biotech products and services in Brazil are taken from a new *survey* realized by the authors for DPP-FINEP research still in course. According to the MCT ´s research report on *Biotechnology and Genetic Resources* (www.mct.org.br/biotecnologia) the market for biotechnology in Brazil corresponds approximately to a share of 2% of the GDP, gathering hundreds of small biotech companies with estimated sales of U$S 2.3 and U$S 3.9 in 2000. In terms of employment, biotechnology creates almost 28.000 qualified jobs in Brazil.

The analysis departs from the point that the biotechnology industry in Brazil is still being constituted. Consequently, it is also still hard to separate public initiatives from private ventures. The DPP survey from 2002 have included around 30 companies that would be really performing in the modern biotechnology business[21].

According to what was previously mentioned, the biotechnological companies in Brazil are mainly focused in the human health and agriculture sectors. The largest share is still in the human health sector representing 26% of the total number of companies. The survey also stresses the importance of the agriculture biotech companies (22%). Considering also the firms that work with the basic tools applied to diagnosis in agricultural and veterinary, this participation becomes even more expressive.

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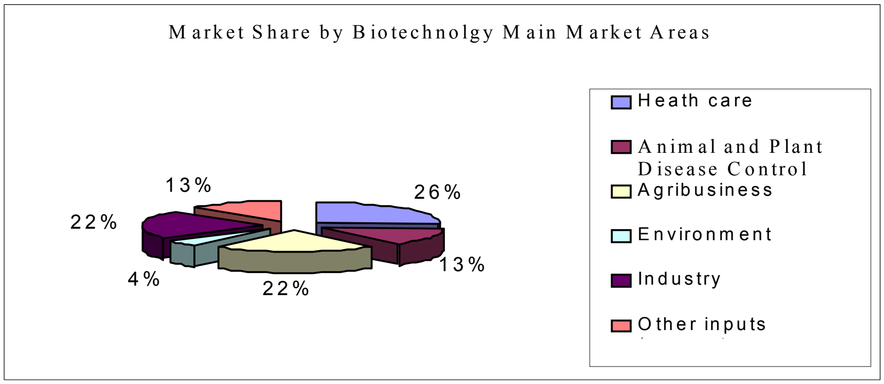
[20] Part of both the MCT and DPP research will be published in a book organized by Silveira, Assad and Dal Poz (2003).

[21] Qualitative enterviws with companies made by the authors in the MCT study authorise our observation.

Figure2- Biotech market-share



Source: DPP and MCT,2003

Most of the companies in the biothech agribusiness tend to specialize in the production of plants with no viruses, inoculants and with the application of techniques that accelerate the process of vegetal improvement like molecular measurers and somatic variation. Other companies deal with vegetable research and improvement to bigger companies. The first companies genuinely specialized in biotechnology in Brazil were Biomatrix and Bioplanta.. These firms were founded with the purpose of supplying with new products and services to the growing industry of pulp and seed producers. The reasons to explain the failure of these ventures are not of technological nature and would possibly be associated to a certain lack of managerial experience expressed in the loss of important technological knowledge that changed to the hands of their customers.

Table 4. Age of Biotechnology Firms in Brazil

Degree of Maturity of Biotech Firms in Brazil		
Age	*Companies N = 23*	
	N	*%*
1 to 3 years - *Start ups* (after 2000)	3	13,0%
3 to 7 yeras - *New Companies* (after 96-before99)	6	26,1%
7 years and more- *Mature Companies* (until 1996)	14	60,9%
Total	23	100,0%

Source: DPP FINEP:2003

DPP survey had selected firms using the criteria of relevant market. According the survey, about 40% of biotech firms in Brazil show levels of income below US$ 1 million per year and other 18%, between R$ 5 million and R$ 12 million. The upper segment in Table 5 shows that 26% of biotech companies are already established with more than US$ 30 million per year. This data confirms that market structure is not concentrated. The MCT and Judice (2003) had found 82 % of biotech firms income under US$10 Million and only 18% over R$ 20 Million. This difference can be explained by the fact that the latter included also small pharmaceutical services and few non- biotech activities.

Table 5- Income of Biotech Firms in Brazil*

Level of Income - DPP Survey		
Level (U$1000)	N= 23	
(without income-investments only)	3	13%
up to 250	5	22%
251 to 1000	4	17%
1001 to 2500	1	4%
2501 to 5000	0	--
From 5001 to 10000	2	9%
From 10001 to 50000	2	9%
More than 50000	6	26%
TOTAL	23	100%

Source: DPP FINEP,2003 (*US$1 = 3 R$)

Table 6 displays income bands in terms of the origin of capital and R&D investments. Among the most profitable companies, 2 are multinational and 3 are national. From the 19 national companies, 9 earn until R$ 1 million and 6 earn over R$ 10 million. More than 80% of the national companies polled declared that they invest in R&D when only 25% of the foreign capital companies do the same in Brazil. This is explained by the fact that R&D investments are realized, in most cases, on autochthonous based branches of the big international groups.

Table 6 – Origin of Biotech Capital and Income Levels*

Origin of Capital	**Yearly Income Levels (in US$ 1000)**	**%**
Foreign Capital		
	From 1001 a 2500	25%
Income	De 5001 a 10000	24%
	More than 50000	51%
Brazilian		
	up to 250	25%
	From 251 a 1000	20%
	De 5.001 a 10000	10%
Income	De 1.001 a 50000	10%
	More than 50000	20%
	n.r.	15%

Source: DPP FINEP 2003 by the authors (1 dollar = 2 R$)

From qualitative interviews with managers and owners of biotech firms, one can identify an evident dependence of biotech firms from public financing trough public incentive. The external source of funds is generally used in infrastructure like equipment, investment in human capital like training academic and for the updating of technicians like biologists and pharmaceuticals. More than 80% of Brazilian companies pretend that they invest in basic R&D. Contrasting, only 25% of international firms have declared to invest in R&D in Brazil. This is not a surprise as international biotech and pharmaceutical companies keep their R&D departments in their matrix research centres. (Table 7).

Table 7 – Biothech companies: origin of capital and R&D investments

Origin of Capital	R&D Investments	%
Foreign	Yes	25%
	No	75%
Brazilian	Yes	82%
	No	18%

Source: DPP FINEP (2003) by the authors

Brazilian biotechnology start-ups companies come from Brazilian universities or governmental laboratories. This is the case of Allelyx, São Paulo, founded by researchers working in the Genoma Project (Xyllela). Allelyxs also received US 12 million from the venture capital Votorantim Risk fund and from Fundecitrus and Coopersucar Allelyxs have two large scale sequencers and 40 researchers developing new biotech approaches to improve plants. Another significant contractor is the Belgian firm Crop Design, also interested in the results of the Sugar Cane Genome, currently studied within the realms of the Consortium sponsored by FAPESP.

Companies financed by venture capital tend to expand in number together with the establishment of new risk capital funds like Votorantim, and Rio Bravo in Brazil. However the former are still dependent on public funds and subsidies. Another very good example of creation of biotech firms from universities is RD Biothech, a company created by researchers and professors from the USP medical school in Ribeirão Preto, São Paulo. The biotech capabilities obtained by RD Biotech are direct consequence of synergies created from experience with recombinant vaccines research to human health, the vaccines for tubercles study and the veterinarian vaccines experience (*Babesia bigemina*).

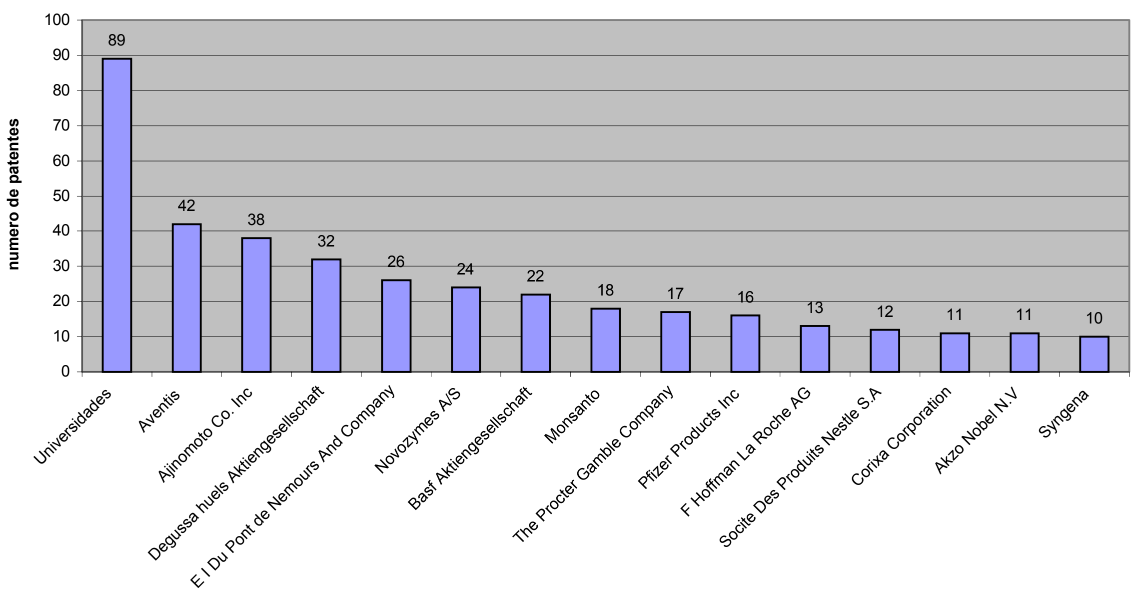
Most of the mentioned companies are still depend on scholarships granted to young students of the graduate area. The researchers also need support to build the necessary infra structure that fit in the *bio-safety* patterns (laboratories with filters, positive pressure and absolutely clean areas). Even more, an emerging company needs to use both the public networks and the consolidated public institutions like Fiocruz, Butanta or Tecpar to realize pre clinic tests.

6. Intellectual Property Rights in Brazil: a glimpse on preliminary data

The protection for invention trough patents in the biotech business is a sort of thermometer of the importance that the Brazilian market has for companies and private agents acting in a global environment. Since the middle of the 90´s Brazil has new rules of institutional game, the Law 9279/1996. The latter defines accurately that transgenic micro-organisms (varieties or micro-organism specimens) are subjected to patenting only if certain perquisites are fulfilled (article 18 of the law). The law states that neither plants nor superior animals are patentable in Brazil. Patents of micro-organisms, however, are clearly allowed to be patented if certain perquisites are followed (article 18, caput III)[22].

Few recent studies on Industrial Property show that the claims for biotech patents in Brazil from international individuals and companies are growing. (Bermudez, 2002; Epsztejn, 1998) According the former study, between 1979 and 1995, 97 patents were registered in Brazil. Between 1996 and 1998, more 186 of patents in modern biotech field were registered. The latter study shows 58 patent claims registered in the traditional biotechnology areas, between 08/92 and 12/95 (60% related to human health area). According Epsztejn, the share of the pharmaceutical claims had grown from 43% to 57% between 1979 and 1998. The figure below is based on INPI databank on patent claims on modern biotechnology survey[23].

Figure 3 – Biggest biotech patent owners in Brazil (1998-2001)



Source: Fonseca and Kimura(2002) using INPI database.

[22] After Brazil had introduced the new industrial property law, in 1996, pipeline protection started to allow new claims on fields that weren't recognized before[22]. From the total amount of biotech patents claims, like 2/3 (147) come from agents located in United States and the rest (52) from Germany, Japan, France and UK. Like 80% of that amount are related to procedures within modern biotechnology, more specifically genetic engineering and mutation technologies (C12 N15 class). These actions are more concentrated in medicinal topics (63%) and modified plants (18%). In a total of 116 firms, the biggest claimers of property rights are: Amgem (18), Monsanto (16), Cyanamid (14),Genetech (12), Du Pont (10),Ajinomoto(9), Dow (6), Sanofi (6), Delkab Sementes (5), A Home Prod. (4), Basf (4), Hoesch (4), Hoffman La Roche (4) and Pierre Fabre (4). Monsanto, Dupont, Ajinomoto and Dalkab´s area of interest is related to agriculture or food industry

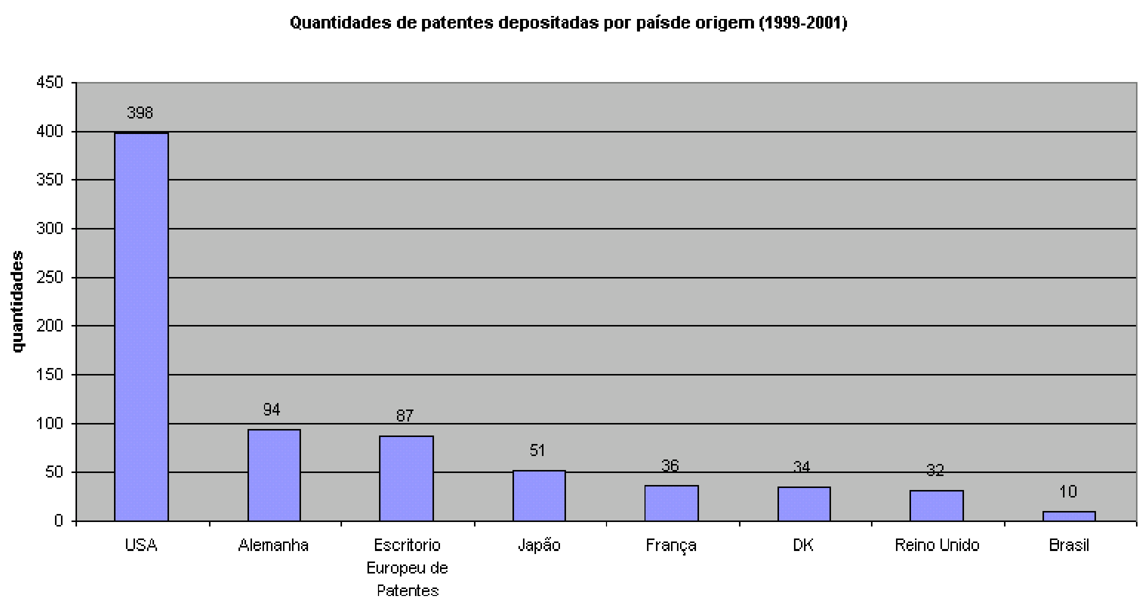
[23] INPI is the National Institute for Industrial Property

As expected, the international and Brazilian universities are at the top of the list followed by Aventis and Ajinomoto, Degussa, Du Pont and Novo. The last chart displays more information on modern biotech patent registration from 1999 till mid 2001. Accordingly, United States is the leader of register s followed by Germany, the EU bureau, Japan, France, Denmark, UK and Brazil.

The study carried by Fonseca and Kimura (2002) also shows that the major share of patents claims is framed in the *New Biotech* field, more specifically in the genetic engineering and mutation techniques (see last chart). In the case of vegetable biotechnology there is a visible trend, like it was mentioned before to the increase in registrations for patents over GM plants. Ajinomoto and Nestlé are isolated exceptions with relative claims about fermentation processes applied to the food field. In the medicine field, the distribution is less concentrated with a small trend towards the peptides.

The study also points out that the interest of foreigners in patenting new biotech plant processes in Brazil is absolutely clear: International companies compete and, at the same time collaborate, through contracts and agreements with Brazilian governmental laboratories. Brazilian start-ups and new biotech companies maintain their own agreements mostly with Brazilian and USA universities to develop scientific and applied research on vegetal biotech, and are now obtaining important funds from Brazilian private venture capital agents.

Figure 4-Patents claims divided by countries (accumulated 1999/2001)



Source: Fonseca and Kimura (2002) using INPI database

7. Conclusions

The economic impacts of the biotech innovations are still taking shape in Brazil. In fact, the transformation of innovations from process to new products and services of commercial viability have been slower than expected. Notwithstanding, the stocks of biothech companies appreciated a lot in the end of the 1990's, beginning of 2000´s enriching a few well informed individuals and investment groups. The young age of the biotechnological industry allied to the deeply radical attribute of its products and services make the competitive processes difficult to be scrutinized and forecasts obscure. Besides, a complicated process of commercialization is configured with the excessive regulation and control over biotech products to be launched in the market.

Market alliances comprising public and private financial funds are being settled with the help of institutional support. In Europe, basic research seems to be supported by governmental funds. The combination of "corporate governance" and credit banking represents an alternative, but stimulating, opportunity for biotech business (Casper&Kettler, 2000). On the other side, the U.S. and U.K. biotechnology seem to be shaped for more liberal market institutions, with the strong presence of the stock market. Nonetheless, one can also observe the burgeoning presence of non- strict market forms in the U.K., like charity trusts, non-governmental organisations and other private organisations, including British super-markets chains.

The role of basic research in Europe was constantly reinforced by centralized institutions engaged in coordinate funding and regulatory recommendations as well as planning programs for representing biotech companies in the government. Until now the financial and institutional solutions adopted by developed countries have not disrupted the emergence of the biotech building blocks of competences and the rise of new specialized companies. We expect the new regulatory issues that have been discussed by international agencies could also do not disrupt the new competitive environment that has been crated for the rise of new biotech companies in countries like Brazil.

These uncertainties could be also summed with institutional and regulatory problems, especially those created by delays on the process of defining the internal intellectual property rights and by the acceptation of global rules of commercial trade by different countries. It is quite unlike, for example, that United States and Europe accept the way Brazil is dealing with the intellectual property rights of essential processes of life, like patenting plant and live organisms. On the other side, generalized forms of biodiversity piracy should be completely forbidden. The discussion of these issues embodies an immense potential for a conflict. The patent contends amongst developed and underdeveloped countries can increase the immense risk and uncertainties already present in the biotech business. At the same time, they could be a source of new opportunities and improvements for the future development of technologies.

Equally determinant for the success of the companies is the regional concentration of companies around technological clusters and sciences parks. There is a lot of good evidence that the biotech business can take more advantage of the proximity with the universities and laboratories where they can closely deal with scientists and share research facilities. The Boston cluster and the Bay Area Valley in San Francisco are good examples of this movement in the USA. The reasons that explain the local agglomeration of these industries are the same to explain the concentration of informatics companies in the Silicon Valley few years ago. The process generally happens in the following way: firs a group of firms settles in a specific area searching for qualified labour or tax cuts/fiscal incentives offered by local or regional governments (similar to what happens in Brazil).

Several biotech clusters have been created in Brazil since the 1980´s. The Bio Rio UFRJ Science Park, in Rio de Janeiro and the BIOMINAS *inland* cluster are amongst the most import initiatives in Brazil. A last factor of success in the case of emergence for new biotech activities can be represented by venture capital offers. In several countries, venture capitals make up for the shortage of subsidy funds in the case of very risky innovation. Peculiarly, despite the fact that some of biotech products have never been place in the market, the Bio-business stock price had a considerable success particularly two or three years ago.

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9. Annex

- Start-ups: RDBIOTEC (Rib. Preto); PRÓ-CLONE, FK-Biotec, Simbios, Hormogen;
- Traditional biotechnology and related areas: Nutriente , Biosoja, Microbiológica, Planta Medicinal, Laborgen, Montecitrus, Probac;
- Average/Large scale: Millenia, Agromen, CELM (equipamentos), Copersúcar, Klabin- Riocell.
- Branches of world leaders: Applied Biossystem;ABX, Mercocítrico.
  Services: Genosys, Biológica, Genomic.

Leader firms in patents race in Brazil: origin and application fields

Group	Number Patents	Origin	Specific Application	Application Field
Aventis	42	US/Germ/Fr	New Plants / Medicaments	Pharmaceutics Agricultural
Ajinomoto	38	Japan	Fermenting Process Enzimes	Food
Degussa	32	Germ	Chem Synt. and Fermenting Process;Enzimes	Chemistry Clinical and Pharmaceutical
Du Pont	26	USA	Novas Plants Medicaments	Pharmaceutical Biologic Material
Grupo NOVO	24	DK	Enzymes	Chemistry Biologic Material
Basft	22	USA/Germ	Novas Plants Enzymes/ Medicament	Agricultural/ Chemical/ Pharmaceutical
Monsanto+Delkab	18+1=19	USA	New Plants	Agricultural
Procter Gamble	17	USA	Detergents in general	Chemistry/Hygiene and Biologic Material
Pfizer+Pharmacia	16+3=19	USA	Hormones and drus(human and animal)	Pharmaceutical
Hoffman-La Roche	13	US/EU	Drugs(human and animal)/ reagents	Pharmaceutical Veterinarian Chemistry
Nestle	12	Switzerland	New Plants	Food
Corixa	11	USA	Medicaments	Pharmaceutical
Akzo-Nobel	11	EU	Medicaments Humans ‘n Animals	Pharmaceutical Veterinarian

Source: INPI by the analisys of the author (2002)