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# THE REGULATORY FRAMEWORK AND THE EFFECTIVENESS OF ALLIANCES IN THE INITIAL STAGES OF DEVELOPMENT OF BIOPHARMACEUTICAL INDUSTRY

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Abstract

The biopharmaceutical industry depends on fragmented knowledge shared out among many different players, prompting companies to engage in contractual strategic alliances. One of the factors shaping the relation among partners in the sectoral system of innovation of biotechnology is the institutional environment, with the regulatory system being one of its key dimensions. This paper conducts an analysis of how the regulatory framework relates to the motivation to engage in alliances and to their effectivenesses in the initial stages of development of this industry. Primary data were gathered from a private association, four government agencies and five biotechnology enterprises in the Brazilian biopharmaceutical industry. Through the categorical thematic content analysis technique, this work proposes that the R&D investment in biotechnology firms, the relationship capabilities of the agents, the broad scope of public investment programs, the operating efficiency of the regulators and the government procurement policies moderate the transformation of public funding in effective alliances.

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## ABSTRACT

The biopharmaceutical industry depends on fragmented knowledge shared out among many different players, prompting companies to engage in contractual strategic alliances. One of the factors shaping the relation among partners in the sectoral system of innovation of biotechnology is the institutional environment, with the regulatory system being one of its key dimensions. This paper conducts an analysis of how the regulatory framework relates to the motivation to engage in alliances and to their effectivenesses in the initial stages of development of this industry. Primary data were gathered from a private association, four government agencies and five biotechnology enterprises in the Brazilian biopharmaceutical industry. Through the categorical thematic content analysis technique, this work proposes that the R&D investment in biotechnology firms, the relationship capabilities of the agents, the broad scope of public investment programs, the operating efficiency of the regulators and the government procurement policies moderate the transformation of public funding in effective alliances.



**Keywords:** sectoral system of innovation, regulatory framework, strategic alliance, alliance effectiveness, alliance motivation.



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## INTRODUCTION

A sectoral system of innovation (SSI) consists of a set of new and established products for a given or emerging demand, characterized by a common knowledge base, and a set of agents carrying out activities and market and non-market interactions through which companies in a sector learn and introduce practices, products, designs and processes that are new to them (Malerba, 2004). The main characteristics of a SSI are its interactive nature and learning curve. A SSI is interactive, to the extent that it involves a system of relationships among assorted players, whose main core factors are: universities and research centers, the State and firms. The first two focus on conducting basic research, and the fourth on applied research. The State plays the role of the agent coordinating the system, encouraging and directing it towards its own demands, generating the infrastructure needed to underpin interactions among the agents, as well as through an industrial policy tailored to technology development guidelines at the national and regional levels. Agents interact through processes of communication, exchange, cooperation, competition and command, shaped by rules and regulations. The learning curve is underpinned not only by formal education and research and development (R&D) activities, but is also encouraged within the corporate environment – learning by using, with more efficient use of complex systems and better market relations; learning by doing, with more efficient production operations; and learning by interacting, through the involvement of the agents and the development of innovative products (Bataglia, Silva, & Klement, 2011). Summing up, the SSI involves three key dimensions: knowledge and technology; players and networks; and institutions.

Regarding the competitive setting for the pharmaceutical sector, it underwent a broad-ranging shift in paradigms with the development of genetic engineering during the 1980s (Powell, Koput, & Owen-Smith, 1996). These new technologies replaced the traditional chemical paradigm of drug discovery and development by a new biotechnological paradigm and paved the way for new players engaged with the sectoral innovation system of this industry: new biotechnology enterprises (NBEs), setting up the new biopharmaceutical sector. The function of these NBEs in the innovation system have been to mobilize the fundamental knowledge created at universities, turning it into prospects with technical potential and sellable products. They also influenced the R&D processes conducted to create new products to become very dependent on knowledge that is fragmented among many different players, such as universities, scientists, research institutes, technical and industry associations, government agencies, NBEs, laboratories, suppliers, customers, and others. This is because the complexity and dynamism of this context have increased significantly. Over time established pharmaceutical laboratories began to encounter difficulties in developing and conducting research in-house, at rates keeping pace with the steady stream of innovations and discoveries. It became quite clear that the competences required by these companies could no longer be developed individually. The integration of NBEs with major pharmaceutical corporations proved the ideal path for their survival. These NBEs began to adopt a cooperative stance as the suppliers of research services to major corporations, which must continually acquire and develop new expertise. In counterpart, major corporations began to provide the NBEs with the funding needed to underwrite R&D activities, as well as the structure needed for the development, testing, manufacturing, marketing and distribution of new products.

These connections between major corporations and NBEs have been established through contractual strategic alliances (Baker, Gibbons, & Murphy, 2003), which have become a new organizational framework for innovative activities in the biopharmaceutical industry, emerging in response to the increasingly encoded and abstract nature of the knowledge base on which innovations are developed (Mckelvy, Orsenigo, & Pammolli, 2004), motivating these organizations to access complementary resources and information and to manage environmental uncertainties (Barney & Hesterly, 1996; Gulati & Singh, 1998; Oliver, 1990). The establishment of property rights over this abstract knowledge made it possible, in principle, to separate the innovative process into different vertical stages, with equally different organizations specializing in specific fields of action: universities at the initial stage, NBEs at the middle stage, and major establishments at the final stage. Along these lines, the creative process may also be considered as a social system, with the locus of innovation lying in the network of inter-organizational relationships (Powell, White, Douglas, Koput, & Owen-Smith, 2005). Contractual strategic alliances grew into channels offering access to new knowledge in this field. The corporate success is related to the capacity of an enterprise to manage its alliances with other companies (Gulati & Singh, 1998; Santoro & Mcgill, 2005), in many different aspects of competitive settings.

Powell et al. (1996) identified a network learning cycle through which participating in the network opens up access to important knowledge that is widely distributed and hard for companies to produce in-house or obtain through market transactions. Organizations conduct different types of transactions through alliances: R&D, clinical trials, manufacturing, licensing/sales, acquisition of rights and supply/distribution. The greater the ability of the firm to

operate within this cooperative network, the more important its role within the relationship network, building up its reputation with enhanced visibility and paving the way for accessing more important information, attracting new talents and setting the pace for the competition. For these players, the biotechnology industry is structured through a network of contractual strategic alliances. Being a key element in a network is necessary in order to attain value-added organizational outcomes (Powell, Koput, Smith-Doerr, & Owen-Smith, 1999). As firms also seek a variety of resources beyond their own boundaries, they develop portfolios of contractual strategic alliances based on relational agreements with specific partners for certain activities.

Estrella and Bataglia (2013) analyzed the influence of the contractual strategic-alliance network on the number of patents filed and the size (number of employees) of 68 Brazilian NBEs in the human health between 2004 and 2008, based on primary data. The findings suggest that as the NBEs build up experience in establishing and managing R&D contractual strategic alliances, they also broaden their access to critical information and resources, developing capabilities with positive effects on filing new patents. The alliance network can lead to the accumulation of expertise in both network and technology management (Souza; Segatto-Mendes, 2008). On the other hand, NBEs working through non-R&D alliances have access to resources such as production capacity, distribution and sales, which underpin larger headcounts.

However, the participation in these alliance networks involves the understanding of a set of cyclic stages, which embraces the relationship building, its maintenance and expansion of transactions among the parties or even its finish in some cases (Boehs; Segatto-Mendes, 2007). One of the factors shaping the relation among partners is the institutional environment linked to the sectoral system of innovation, with the regulatory system being one of its key dimensions

(Malerba, 2004; Pierson, 2006; Viotti, 2002). Relationships and interactions among players, including contractual strategic alliances, are influenced by contextual factors established through government regulations, creating competitive demands to which organizations must respond, in order to ensure their survival and attain their goals (Bataglia & Meirelles, 2009).

This paper strives to offer a contribution through exploring how the regulatory system relates to the motivation to engage in contractual strategic alliances and to their effectivenesses in the biopharmaceutical industry in the initial stages of development of this industry. The selection of the Brazilian economy as its backdrop was prompted by the opportunity to study the proposed research problem. Brazil industrial policy encompasses the biopharmaceutical industry, with specific regulations for this sector established since the early 2000s. Brazilian bioindustry already accounted for some 3% of the nation's GDP in 2008. Looking ahead to shrinking revenues brought in by their portfolios of medications, and faced by the impossibility of copying patented medications due to the Intellectual Property Act promulgated in 1996, Brazilian laboratories launched a drive over the past few years to ensure the feasibility of their initiatives linked to Research, Development and Innovation (RD&I), intending to apply for their own patents by the end of this decade. It completes the opportunity for the study the expansion of the biopharmaceutical industry and of the contractual strategic alliances in this sector in Brazil (Estrella & Bataglia, 2013; Biominas & PWC, 2011).

This paper opens with an overview of the Brazilian pharmaceutical industry. Next comes an introduction to the regulatory system in this field in Brazil, followed by an explanation of the methodological procedures used in this paper. The findings are then presented and analyzed, closing with the final conclusions of this work.

## THE PHARMACEUTICAL INDUSTRY IN BRAZIL

The Brazilian pharmaceutical industry was dominated by major multinational laboratories through to the late 1990s, which opened up companies to produce and sell their wares, attracted by the potential of the densely populated Brazilian market. Stages with more sophisticated technological content – such as R&D and production of the raw materials needed to fabricate these medications – generally remained in their countries of origin. Particularly from the 1990s onwards, after the Brazilian market was deregulated and its currency rose in value, the significance of the production chain established in Brazil shrank to even greater extent, with this sector becoming heavily dependent on imports. This context was also shaped by limited investments in R&D of medications in Brazil, which refused to acknowledge patents between 1969 and 1996, when the Intellectual Property Act was promulgated (Law Nº 9,279). The Brazilian pharmaceutical industry, and more specifically companies with local capital, were encouraged to invest in production through the promulgation of the Generics Act (Law Nº 9,787) in 1999. This Act allowed a benchmark medication (branded) to be substituted by a similar remedy produced after expiry of the patent, with proven efficacy, safety and quality. Supplies of products at more competitive prices, even if not innovative, allowed this sector to take over a larger market share. On the supply side, the Brazilian pharmaceutical market has altered significantly over the past few years. According to the Brazilian Pharmaceutical Industry Federation (FEBRAFARMA), the Brazilian pharmaceutical market ranked tenth worldwide (retail pharmaceuticals) in 2005 with revenues of US$ 11.1 billion, brought in through sales of 1.61 billion units. It is estimated that there are some 500 laboratories operating in Brazil. This

sector has become more densely concentrated, with local laboratories taking over a generous portion of the Brazilian market that was previously held by the multinationals. Brazilian companies that accounted for some 28.2% of medication sales by value in 2000, had already stepped up their share to 40.6% by March 2005 (Capanema, 2006). The trend towards larger market shares held by Brazilian laboratories is also reflected in the fact that the largest Brazilian laboratories intend to file patents for new products during the current decade.

According to the study conducted by the Biominas and PWC (2011), Brazil's bioindustry posted revenues of some US$ 402.1 million in 2008, equivalent to some 3% of the nation's GDP, with a total of 253 companies. This study stresses the current dynamics of this industry, characterized by micro and small enterprises with very trim structures. Around 44.4% of the Brazilian companies post annual revenues of minus than US$ 0.5 million; 47.7% of the companies employ less than ten people, with 72.7% of them having less than twenty employees. Most of the companies are relatively young, with this sector expanding rapidly: 67.7% of these companies were set up during the past decade; 35.4% of them have been in operation for between five and ten years; 19.8% of them were established three to five years ago; and 12.5% of them started up operations within the past two years. Between 1999 and 2003, an estimated ninety new enterprises were set up, more than the eighty companies already in operation. During the next five years, a further 83 were established, reflecting the rapid expansion of this sector, with 20% of these companies active in the human health segment. Southeast Brazil is particularly noteworthy for this segment, with 71.9% of these companies: São Paulo (37.5%) and Minas Gerais (27.7%) States are home to most of these companies, with the city of Belo Horizonte in Minas Gerais being the main urban hub, with 48 companies. University incubators

are turning out a steadily increasing number of biotechnology companies in several Brazilian States, with incubated biotechnology start-ups accounting for 19% of the industry total. Access to new technologies was not considered as a significant problem for most of them, with 73% of these companies having established R&D contractual strategic alliances, in addition to in-house R&D activities. Nonetheless, there is a lack of qualified professionals, and much difficulty with aspects related to business expertise. How to obtain funding, regulatory issues, and matters related to intellectual property were mentioned as relevant.

## REGULATORY SYSTEM FOR BRAZILIAN BIOPHARMACEUTICAL INDUSTRY

In order to characterize the type of protection offered to biotechnology, it is necessary to ascertain the purpose of such protection, in order to then identify the protection tool (patent or improvement right). In the human health segment, as the biotechnology purpose to be addressed consists of genetically modified micro-organisms, the importance of Brazil's Patents Act is confirmed. There is no specific provision in the Intellectual Property Act (Law Nº 9,279/96) on granting biotechnology patents. However, a construal of the law and the regulatory precedents, as well as international influence, means that a patent is normally applicable to a new biological material, invented in the laboratory, if, and only if, the micro-organism meets the requirements of novelty and industrial applicability. Processes are patentable when related to the transformation of plants, recombinant genes and vectors, recombinant proteins, transgenic micro-organisms and pharmaceutical compositions containing extracts isolated from plants for the treatment of a specific disease.

With regard to public policies, from the 1950s through to the early 1990s, as industrialization grew more important in the Brazilian economy, a horizontal approach prevailed for Brazil's industrial policy, grounded on linear tariff reductions and the absence of policies for specific sectors (Barbosa, Mendes, & Sennes, 2007). However, during the 1990s, specific initiatives were implemented through public policies focused on specific sectors whose activities were rated as important for national development. The sectors targeted by public policies in order to foster Brazil's industrial development include the biotechnology and pharmaceutical sectors. The main actions underpinned by public policies with impacts in these two sectors are: government purchases; science and technology programs; Sector Funds; industrial, technology and foreign trade policies; and the national biotechnology policy.

Government purchases in Brazil are a tool deployed by the State to distribute medications among the population at large, starting in 1971. Today, government purchases of medications are encompassed by the pharmaceutical aid program run by the Ministry of Health which guides the acquisition of medications, taking into account the basic healthcare programs offered by the government through Brazil's Unified National Health System (SUS), including immunization, medications for chronic diseases that are expensive for the population in general and the strategic medications program for neglected diseases and AIDS. Competitive bidding procedures favor purchases of medications produced by government laboratories (Bastos, 2006). Furthermore, the Generics Act stipulates that for government procurement purposes, generic medications will be preferred over other alternatives, when available, under equal price conditions. Its impacts on industrial policy is due to the importance of the total value of medications sold in Brazil, accounting for 25% of the total market in 2008, with annual outlays of around US$ 3.6 billion

(US$ 2.6 billion by the Federal Government + US$ 1.0 billion by the States and Municipalities), according to date released by Brazil's Public Health Regulator (ANVISA).

In order to foster the development of science, technology and innovation in Brazil while consolidating the National Innovation System, the Ministry of Science and Technology (MCT) has been implementing science and technology programs for the past forty years that are intended to provide institutional and financial backing for universities, researchers and technology-based companies. The Sector Funds were set up during the late 1990s, in the wake of an abrupt shift in Brazil's pharmaceutical sector policy, moving away from its horizontal approach to focus on the specific needs of this sector and stressing the promotion of innovation as a way of enhancing the competitive capabilities of Brazilian industry (Barbosa, Mendes, & Sennes, 2007). Established from 1999 onwards by the Brazilian's Studies and Projects Financing Agency (FINEP), the Sector Funds are tools for financing research, development and innovation projects, constituting supplementary sources of funds for underwriting the development of sectors that are strategic for the nation. The revenues of these funds consist of levies payable on the outcomes of exploiting natural resources owned by the Central Government, portions of the Industrialized Products (IPI) tax in certain sectors, and the Royalty and Licensing Fees (CIDE) due on the amounts paid in as remuneration for the use or acquisition of technological expertise and technology transferred from abroad. The management model designed for the Sector Fund is based on Administration Committees, with one allocated to each fund. Each Administration Committee is chaired by a representative of the Ministry of Science and Technology (MCT), with its other members consisting of representatives of related Ministries and regulators, in addition to academic and business sectors, in addition to the

agencies of the Studies and Projects Financing Agency (FINEP) and the National Council for Scientific and Technological Development (CNPq).

There are sixteen Sector Funds, with fourteen covering specific sectors and two cross-sector funds. The Sector Funds related to the pharmaceutical chain are the CT-Health and the CT-Biotechnology. The more important in terms of its budget allocations, the CT-Health fund builds up technological capacities in areas of interest to Brazil's united National Health System (SUS): healthcare, drugs, biotechnology, etc., in addition to encouraging heavier private investments in R&D, with technological updates for the Brazilian medical and hospital equipment industry, and the dissemination of new technologies that expand access for the population at large to goods and services in the healthcare area. The CT-Biotechnology fund underpins the training and capacity-building of human resources for the biotechnology sector; strengthening Brazil's research infrastructure and support services; expanding its knowledge base; encouraging the incorporation of biotechnology start-ups and technology transfers to companies that are already consolidated; in addition to prospecting and monitoring the progress and knowledge in this sector.

In general, the Sector Funds allocate financing to projects selected through public calls for submission, whose announcements are published on the internet portals of the Studies and Projects Financing Agency (FINEP) and the National Council for Scientific and Technological Development (CNPq), as well as through partnerships with the State, Science and Technology Bureaus and their Research Support Foundations (FAPs).

In March 2004, the Industry, Technology and Foreign Trade Policy (PITCE) was launched, which selected the medications sector, and more specifically biotechnology, as one of

the four strategic sectors rated as technical process disseminators, where Brazil posts a significant trade deficit, with an appreciable lag in competitive terms. Through this approach, technological innovation is assigned a key position, being viewed within a context of modernizing and expanding production capacities, in parallel to investments in R&D and more dynamic performances on international markets, including programs underwriting these activities. Since it was launched, this Policy has played a leading role in steering the actions undertaken by an assortment of government programs that were previously deployed individually by various Ministries.

In February 2007, Brazil's Biotechnology Development Policy (PNB) was established, mainly in order to endow domestic industry with keener competitive edge, striving to identify demands and create tools that can turn the knowledge accumulated in universities into industrial output. In order to manage public policy in this area and define its priorities, the National Biosecurity Council (CNBS) was established, together with the National Biosecurity Technical Commission (CTNbio), coordinated by the Ministry of Development and consisting of representatives of the Presidential Staff and the Ministries of Health, Science and Technology, Agriculture, Environment, Education, Agrarian Development and Justice. This Committee also includes entities connected to the research development, such as the National Council for Scientific and Technological Development (CNPq) and the University Level Staff Higher Education Coordination Unit (CAPES). Institutions that provide project financing, such as the BNDES (Brazilian Development Bank) and FINEP (Studies and Projects Financing Agency ) also sit on the CTNbio.

## METHODOLOGICAL PROCEDURES

The general goal of this study is to analyze how the regulatory system in the biotechnology industry relates to the motivation to engage in alliances and to their effectivenesses in the initial stages of development of this industry. Particularly the Brazilian biopharmaceutical industry was study. Three specific goals were set. The first specific goal was to research the regulatory, technology and market aspects that characterize the Brazilian biopharmaceutical industry. This was divided into two stages: the first examined secondary documentation and conducted a review of the bibliography, while also identifying biotechnology companies in this sector. During the second stage, interviews were conducted to obtain primary data from four government agencies and one sector association.

The second specific goal was to categorize the contractual strategic alliances established by five Brazilian biotechnology companies (NBEs) between 2007 and 2009, based on primary data. These firms were selected through the information obtained under the first specific goal. The selection criterion consisted of having active contractual strategic alliances during the past five years. Two-tier analysis was used, defined by two core dimensions of the sectoral-system-of-innovation construct: the institutional system and relationships among agents. The institutional system analysis tier was operationalized by the biotechnology industry regulatory system, including legislation and public policies (Del Nero, 2008; Malerba, 2004; Pierson 2006), while the agent relationships examination tier was operationalized by contractual strategic alliances set up through formal agreements among agents (Powell et al., 2005). It was considered for each alliance: its type (Powell et al,, 1996); its motive (Oliver, 1990; Gulati & Singh, 1998); and its effectiveness, defined as the reach of its initial strategic objective (Schilken & Goerzen,

2010). Categories were defined a priori for each analysis tier, based on a review of the bibliography and secondary documents related to the Brazilian biopharmaceutical industry. The categories established for the analysis tiers are presented in Table 1.

<Insert Table 1 about here>

The sector organizations and the NBEs were invited to take part by email messages, listing the requirements for participation. Basically, the intention was to discover how the managers perceived the proposed analysis tiers, obtaining primary data linked to the first and second specific goals through in-depth interviews. The indicators used for each analysis category and the interview guides were established through the review of the bibliography and secondary documentation. All the indicators were explored through open-ended questions, with the questionnaire prepared for the interview with managers of sectoral organizations differing from that used for the managers of the NBEs. The former focused on their perceptions of the general characterization of the indicators for the biopharmaceutical industry, while the latter focused on the perceptions of the managers for the characterization of the indicators based on the experiences of their companies in the contractual strategic alliances under examination.

The collected data were transcribed and run through a thematic analysis by category (Bardin, 2000), using the multiple case strategy (Yin, 1994). It was attempted to reduce the number of distortions and gaps in the memories of the respondents in two ways. The first was to establish a period between 2007 and 2009, while the second was to prepare a descriptive summary with a synthesis of the interviews of each organization, which was then validated by

the managers. Whenever possible, more than one interview was conducted. When discrepancies were noted among the descriptions provided by the respondents, additional telephone interviews were conducted in order to reconcile the information. The interviews were held in the organizations, with the respondents at the NBEs being first and second level managers. Second level managers were associated with the R&D and market organizational functions. For the government agencies and sector organizations, the criterion was that the respondent should be linked to areas working with the biopharmaceutical industry. This step was designed to ensure the integrity of the information, while avoiding biased perceptions caused by the areas in which the managers worked. The interview guide was pre-tested with a government agency and a biotechnology company.

The third specific goal was to generate tentative, non-definitive propositions on the relationship between the regulatory system of the biopharmaceutical industry and contractual strategic alliances between 2007 and 2009, corresponding to the descriptions of the alliances and the experience built up in partnership management, grounded on regulatory aspects. Each case was analyzed individually, and subsequently together. The descriptive summaries of each case were studied, and the data collected during the interviews were run through thematic analyses by category (Table 1). Then the explanation construction tactic was used in a cross-analysis of the cases (Eisenhardt, 1989). The explanatory propositions were generated through classifications and comparisons. Subsequently, these propositions were compared with each of the cases in order to ascertain whether the data confirmed the proposed relationships, and if so, this would lead to a better understanding of the current dynamics. The propositions generated by the inductive process were then fine-tuned through the existing literature.

## FINDINGS AND ANALYSES

As set forth in the research methodology presented in the previous section, organizations were contacted by email, with all of them agreeing to participate in this survey. The five biotechnology enterprises are under Brazilian control, with at least three active strategic alliance agreements under way between 2007 and 2009. NBE1 has three R&D partnerships with universities and one with a supplier, as well as a manufacturing agreement with a licensing customer. NBE2 has two venture capital partnerships with government agencies, one R&D agreement with a university, another agreement covering R&D activities and clinic trials with another university and a distribution agreement with a Brazilian distributor. NBE3 has one R&D partnership with a university, two consulting agreements with a state university incubator and a government agency, and two distribution agreements with one supplier. NBE4 has one R&D partnership with a federal university, one venture capital partnership with a government agency, and one distribution agreement with one supplier. NBE5 has two R&D partnerships: one with a federal university and one with an Argentinean company; and two partnerships with suppliers. Table 2 presents the profiles of the organizations and the managers who took part in this survey. The propositions presented below were generated through the evidence analyzed.

<Insert Table 2 about here>

Access to complementary resources, obtaining outside information and the inter-organizational learning curve are major motivational factors prompting biotechnology companies

to set up contractual strategic alliances. This kind of incentive to alliances was listed by Barney and Hesterly (1996), Oliver (1990) and Gulati and Singh (1998).

> We have research and development [agreements] with the Rio de Janeiro Federal University and the University of São Paulo and with companies outside Brazil. We gain through knowledge and access to laboratories and specialists. This is very important. (NBE1)
>
> We developed the FINEP project with a partner. We learned a lot together. This is very important. For them [FINEP] to pay in capital, they assess our project and this is already a learning curve that helps us fine-tune the project and ensure that it is really sturdy and complete, that includes everything required. (NBE2)
>
> We basically have an office structure, because we did not want and cannot invest. But if we could, I think we would not invest in a large laboratory structure, because it implies a fixed cost, which we do not yet have the resources to maintain. (NEB5)

Formally,

**Proposition 1 (P1).** The motivation for biopharmaceutical companies to make use of public financing in order to develop innovation projects via contractual strategic alliances is linked to access to resources, information and inter-organizational learning curves.

However, companies in the biopharmaceutical industry encounter operating difficulties with the absorption of intellectual property resulting from innovative activities, stepping up uncertainties and the amounts allocated to investments in innovation. The operating difficulties

encountered in the ANVISA registration procedures, as well as the administrative procedures of the INPI and the CTNbio, the requirement of prior assent from ANVISA for publishing patents granted by the INPI and the limited experience of ANVISA specialists lengthens leadtimes, with increased uncertainty and higher risks associated with investments in innovation, thus delaying the market penetration of biotechnology-based remedies.

> [On the Biosecurity Act] Now, this is another black hole, because anyone who submits the paperwork there has no idea about what will happen, and the times are really long. (SO1)
>
> ANVISA, for us, is a bogeyman, because we as a small company, we do not have capital to wait years until they release a product of ours that is ready. When they let you go, the product is not new anymore. (NEB2)
>
> So this is a huge disincentive, actually [...] this is my relationship with the INPI, we filed a patent there and she disappeared ... It takes ten years and nothing. (NEB1)

Operating difficulties with decisions on patents undermine the appropriability of the technological environment, hampering the transfer of biotechnology and biochemistry from the academic arena to the business field, obstructing private financing and making it harder for companies to go public. The same situation occurred in US throughout the 80's. The approval process by the FDA was slow and incremental (Ryan, Freeman, & Hybels, 1995). The problem was solved only by Congress' regulation. This situation consequently encourages public financing and the establishment of partnerships, in order to offset and share risks (Gulati & Singh, 1998). Furthermore, weaker appropriability may encourage the appearance of independent local monopolies and wider markets connections (Malerba & Orsenigo, 1993).

Formally,

**Proposition 2 (P2)**. Operating problems with the regulators working with Intellectual Property, registration control and biosecurity make it harder to obtain rights over intellectual property resulting from innovative activities, downgrading the project risk profiles and delaying the market penetration of biotechnology-based medications.

More funds have become available for science, technology and innovation in Brazil over the past few years. In the views of the managers, company access to government funding for financing and investing in innovation has been curtailed by the limited quantity and poor quality of the projects presented.

> In our view, there is plenty of money available today. Look, FINEP [Studies and Projects Financing Agency] has just released the figures for its allocations this year, with 2,500 projects already presented. But even so it has a budget of US$ 225 million for allocation, and is unable to do so. (SO1)
>
> The problem is not so much the amount of funding around, the issue is the quality of the projects. (GA1)

It seems that this problem is related to a lack of investment by the companies, which do not employ scientists and do not set up research and development areas. The Ministry of Science and Technology (MCT) is in charge of establishing policies for the science and technology area,

historically focusing on training researchers in universities, mainly through the National Council for Scientific and Technological Development (CNPq). During the past few years, this entity has made a point of expanding the scope of its activities through establishing public innovation policies for Brazil, such as the National Biotechnology Policy, which is designed to train a highly skilled work force. However, these policies are apparently unable to place employees with master and doctorate's degrees in the companies. This means that good projects are in short supply, for seeking out the available funding, which may result in amounts not allocated through competitive bidding procedures being channeled back to the Treasury.

> A very serious problem is that companies do not innovate. And why do they not innovate? Because they lack R&D, they have no scientists, they barely have an engineer. So this is a really serious problem, because you do not have adequate projects. (GA3)
>
> One of the goals was to create a critical mass. They [CNPq] managed to qualify a large number of people in Northeast Brazil, with master's degrees and PhDs. It is all very well, conducting research, but when is this research going to the market? (SO1)
>
> Now what it [MCT] needs to do is to make sure that people with master's degrees and PhDs reach the companies. (NBE1)

The managers stressed the dependence of the companies on universities, resulting in companies being located close to these organizations.

> It is very hard for a company to set up an R&D center today, so it will certainly be dependent on partnerships with research institutions. Even major companies end up close to major research centers, where they can access resources, at least part of the human resources. (GA1)

> 80% of everything under way in Brazil is at universities. In the more developed countries, the applied research is handled by enterprises, leaving basic research to universities and research institutions. (GA2)
>
> Most researchers in Brazil are in universities and government research institutes. (NEB4)
>
> Partnerships with public universities are strategies for reducing risks. (NEB5)

Formally,

**Proposition 3 (P3).** The relation between available public funding for innovation and good quality projects via effective alliances is moderated by the R&D investments allocated by companies, including permanent jobs for people with master's degrees and PhDs on their staffs.

When analyzing the support offered to micro-enterprises, there is clearly still a gap throughout the entire set of financing programs, which increases the risk of microenterprises going bankrupt, being bought out or switching focus, in order to survive. The actions of the BNDES (Brazilian Development Bank) seem to have little effect on financing for biotechnology companies, as it focuses on larger-scale projects.

> The amount of more than US$ 0.5 million to go directly to the BNDES is high for small companies. In fact, there is a very small universe of biotechnology companies that obtain financing directly from the BNDES. (NBE2)

> The BNDES is a bank that does not have an in-house structure appropriate for dealing with small companies. Traditionally, this development bank has always worked with massive projects, huge infrastructures. It lacks the structure to move ahead in this field. (GA2)
>
> There is a stage in the financing production chain where there is a black hole that we have not yet covered. So it is very common for you to see that a company either closes down, or it is very good and is bought out by somebody, or it loses its focus, because it must survive. (GA3)

Formally,

**Proposition 4 (P4).** The relationship between the availability of public funds for financing and investment in innovation and good quality projects and effective alliances is moderated by the scope of financing programs, in terms of the various growth phases of an innovative enterprise.

On the other hand, there seem to be difficulties in relationships among NBEs, universities and research institutes, in terms of setting up alliances. Universities lack mechanisms for managing relationships with companies, and companies usually are unaware of how universities function. This result coincides with that obtained by Segatto and Cruz (2009).

> The company is still unable to deal with the institutional aspects of the university. Very few universities have mechanisms for administering partnerships between universities and companies. I mean that there are few people who can handle these two worlds, who can bring these two worlds closer together and build up a formal partnership. (SO1)

> In other words, the purpose of universities and scientists is the eternal progress of knowledge, while the goal of the company is to bring in profits, always looking at the bottom line. This difference in interests and time-related goals between the company and the university lies at the base of the main difficulties. (GA3)
>
> Then the relation business-university is very difficult. The company wants the result for tomorrow and the researcher wants the result to two years from now. (NEB3)

Formally,

**Proposition 5 (P5).** The relationship between the availability of public funds for financing and investment in innovation by the NBEs and good quality projects via effective alliances is moderated by the relationship skills of the partners.

Government purchases represent an area of public activity with significant potential for developing the biotechnology sector. Apparently, government purchase policies are not yet clearly delineated, with this purpose.

> What we see is that every time the government indicates it wants to run a project that will provide leverage for a product and there is a company that is interested in the development in order to sell to the government, every time this starts up, a government research entity appears and says: "no way, I do that". And it ends up buying from the Federal entity. (SO1)
>
> We sign up for public tenders run by some government hospitals that end up by buying large volumes. Although the price normally goes way down, because this is always conducted through competitive

> bidding procedures. Even if someone offers an inferior product, they still force the price down. But this is an important sale. (NBE2)

Formally,

**Proposition 6 (P6)**. The lack of a clear policy assigning high priority to innovative Brazilian NBEs in public purchases curtails the use of government financing available for partnerships and innovation in biotechnology industry.

Summing up, the proposition's relationship model is presented in Figure 1.

<Insert Figure 1 about here>

The reasons prompting biopharmaceutical companies to make use of government financing in order to develop innovation projects via contractual strategic alliances are steered by the need to access resources and information, as well as inter-organizational learning curves (P1). However, operating problems in the regulators may hamper private financing and prevent companies from going public, encouraging government financing and the establishment of partnerships as strategies for reducing or even eliminating risks, encouraging the appearance of local monopolies and interconnected markets (P2). The link between the availability of government funds for financing and investing in innovation at the NBEs and good quality projects and effective contractual strategic alliances is moderated by the level of investment in

R&D among the NBEs, including permanent employment of qualified staff (people holding master's degrees and PhDs) at the NBEs (P3), the availability of financing programs that respond to the various growth phases of the NBEs (P4) and the relationship skills of the partners (P5). The lack of a policy clearly assigning priority to innovative NBEs with Brazilian stock control for government purchases, including government enterprises, curtails the use of the available public financing for establishing partnerships and projects focused on innovation (P6).

## FINAL REMARKS

The purpose of this paper is to examine relationships between the regulatory system and the effectiveness of contractual strategic alliances in the biopharmaceutical industry in the initial stages of development of this industry. Particularly the Brazilian biotechnology industry was studied. This purpose was achieved, concluding that biopharmaceutical companies are incentivized to make use of government financing to develop innovation projects via contractual strategic alliances by the need to access resources and information, as well as inter-organizational learning curves.

Nonetheless, operating problems in the regulators may hamper the registration of intellectual property rights resulting from innovative activities, blocking private financing and preventing companies from going public, while encouraging government financing and the establishment of alliances as strategies for reducing risks. It seems that this situation partially explains the paradox that has appeared in Brazil's biopharmaceutical industry during the past decade. If on the one hand public funding has become more available for financing and

investing in innovation at companies, on the other, access to these fund has been curtailed due to the poor quality and limited number of projects presented. Furthermore, it is possible that the shortage of well-qualified projects is also associated with the size of the NBEs, where micro and small enterprises prevail, lacking qualified staff and adequate research infrastructure. The importance of incubators is stressed, as they can help enhance company qualifications through providing guidance on the availability of financing programs, indicating how to access them and listing their quality requirements. On the other hand, qualified work force generation programs and policies at the master's degree and PhD levels, require supplementary policies that encourage permanent jobs for highly qualified staff at these NBEs, particularly during the initial product or technology development phases, through to market launches. Through this approach, NBEs would build up their capacities to generate well-qualified projects that would allow them to access resources, in terms of capital as well as research infrastructure, through alliances.

Another constraint on alliances between NBEs and universities lies in the very different views of these agents, in terms of innovation and research, as well as the lack of the necessary skills and knowledge required to deal with the organizational structures and the deployment of contractual strategic alliance mechanisms among them. Consequently, the importance of relationship skills-building programs is stressed, which can help enhance the qualifications of companies, universities and research institutes.

In turn, gaps in financing programs for NBEs that are not yet large enough to continue operating alone seems to be a moderating factor in the transformation of public financing in good quality projects, effective partnerships and innovations. The ability to influence public purchases is also apparent in the intensity of these relationships. A policy is required that clearly assigns

higher priority to innovative private companies with domestic stock control, even over other State-owned enterprises.

These findings offer solid contributions, as earlier studies of contractual strategic alliances in biopharmaceutical industry have presented propositions and drawn conclusions on alliance dynamics, although without relating them to aspects of the sectoral system of innovation (e.g., Pisano, 1991; Powell & Brantley, 1992; Powell et al., 1996; Powell et al., 2005). As a methodological contribution, the research design proposed in this paper measured and related two dimensions of the sectoral system of innovation construct: institutional environment (regulation) and player networks (contractual strategic alliances). Along these lines, the paper offers an original contribution to the field.

It is worthwhile stressing that, due to the methodology adopted, the propositions resulting from this paper must be understood as tentative rather than definitive hypotheses. Another limitation of this paper is that although acknowledging that strategic alliances among the players may also be set up informally, they are addressed in this paper according to Powell et al. (2005), considered as formal partnerships. It is also worthwhile stressing that institutions were considered only in terms of their legal and public-policy dimensions.

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## TABLE 1

## Analysis Tiers and Categories

| Analysis Tiers | Analysis Categories | | Source |
|---|---|---|---|
| Contractual strategic alliance | Characterizing factors | Type; motivation; effectiveness. | Powell et al. (1996); Oliver (1990); Gulati & Singh (1998); Schilken & Goerzen (2010). |
| Regulatory system | Legislation | Intellectual property; price control; registration control; taxes; biosecurity. | Del Nero (2008); Malerba (2004); Pierson (2006). |
| | Public policies | Government financing; public purchases; personnel capacity-building. | |

## TABLE 2

## Profiles of Organizations and Managers Participating in the Research

| Organizations | Time on the market (years) | Respondents | Manager experience in the industry (years) | Position | Tier |
|---|---|---|---|---|---|
| Sector Organization 1 (SO1) | 10 | 1 | 15 | CEO | 1 |
| Government Agency 1(GA1) | 58 | 2 | 1.5 and 2 | Biotech Analysts | 4 |
| Government Agency 2 GA2) | 43 | 1 | 9 | Biotech Analyst | 4 |
| Government Agency 3 GA3) | 47 | 1 | 3 | Engineering Director | 2 |
| Government Agency 4 (GA4) | 25 | 1 | 15 | Biotechnology Coordinator | 3 |
| NBE1 | 35 | 1 | 20 | R&D Director | 2 |
| NBE2 | 8 | 2 | 12 and 12 | CEO<br>VP | 1<br>2 |
| NBE3 | 5 | 1 | 5 | CEO | 1 |
| NEB4 | 8 | 1 | 8 | CEO | 1 |
| NEB5 | 3 | 1 | 18 | CEO | 1 |

**FIGURE 1**

**Proposed Conceptual Framework for the Relationship between the Regulatory System and Alliances in the Initial Stages of Development of the Biopharmaceutical Industry**