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Technological Cooperation Networks at Bio-Manguinhos: the Role of Information and Communication Technologies

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ABSTRACT

This article identifies and discusses the contribution of information and communication technologies (ICTs) to the technological cooperation projects of Bio-Manguinhos, a pharmaceutical manufacturer that belongs to Osvaldo Cruz Foundation (FIOCRUZ), responsible for producing vaccines, reagents and biopharmaceuticals, with priority on meeting the needs of the Brazilian public health system. It is a case study with a qualitative approach for descriptive and explanatory purposes. The data were collected from 14 interviews conducted with managers of research and development (R&D) projects with high relevance to the organization. The results allow concluding that the ICTs requiring greater interdependence between partners and two-way knowledge flows have not yet been used. They also show the importance of closer cooperation between the information technology (IT) and R&D areas. A future positioning of Bio-Manguinhos as a technological center focused on discovery and sale of new active ingredients can favor the use of tools that promote greater integration between the partners of technology cooperation networks.

Keywords: Technological innovation. Research and development. Information and communication technologies. Technology cooperation networks.

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1 INTRODUCTION

A key characteristic of the chemical companies that gave rise to today's pharmaceutical firms was control of all the steps of the productive chain, including the structuring of professional research and development (R&D), aimed at the creation and protection of intellectual property (IP) (CHESBROUGH, 2006).

The logic for generating revenue of the large global pharmaceutical companies formerly was to keep the intangible assets, consisting of the knowledge generated in the pharmacology and chemical synthesis processes, i.e., the IP, internal until the active ingredients discovered in the experiments could be converted into new drugs with patent protection. This logic was called by Chesbrough (2010, p. 356) the "blockbuster business model."

The advent of modern biotechnology, involving the use of genetic engineering, molecular biology and biochemistry to discover and produce drugs, has dramatically changed the process of technological innovation in the pharmaceutical industry (CHIARONI; CHIESA; FRATTINI, 2008; MALERBA; ORSENIGO, 2001). In face of the rising costs and long time frames, partly caused by stricter regulatory requirements, and in face of the impossibility of detaining all the knowledge involved in scientific discoveries in molecular biology, technological cooperation network arrangements and open R&D management models are coming to the fore in the pharmaceutical industry (POWELL et al., 2005; HUGHES; WAREHAM, 2010).

Molecular biology, especially experiments into the structure and function of genetic material and their expression products, proteins, is a field of knowledge that has particularly relied on the intensive use of computers starting in the 1960s (CATANHO; MIRANDA; DEGRAVE, 2007).

With the preponderance of collaborative models, studies carried out since the mid-1990s have brought evidence of the growing importance of information and communication technologies (ICTs) to the management of the information produced by the R&D process (CHESBROUGH, 2006; ROTHWELL, 1994). Research has also indicated that ICTs contribute to the virtualization of the innovative process itself, reducing the duration and costs of R&D projects (DOGSON; GANN; SALTER, 2006; PITASSI, 2012; THOMKE, 2003; VERONA; PRANDELLI; SAWHNEY, 2006), including technologies for dynamic modeling of molecules and proteins (MCGUFFEE; ELCOCK, 2010).

This study falls in the field of research into the use of ICTs to support technological innovation in innovation and learning networks. We extend this field of scientific investigation seeking to answer the following question: What is the contribution of ICTs to the technological cooperation projects in which Brazilian pharmaceutical organizations are currently involved? More specifically, our objective is to identify and discuss the contribution of ICTs to the technological cooperation projects of Instituto de Tecnologia em Imunobiológicos, or Bio-Manguinhos, a pharmaceutical company belonging to Osvaldo Cruz Foundation (FIOCRUZ) that is responsible for producing vaccines, reagents and biopharmaceuticals, targeted with priority to meet Brazilian public health demands.

2 THEORETICAL FRAMEWORK

2.1 TECHNOLOGICAL INNOVATION IN PHARMACEUTICAL ORGANIZATIONS

The biotechnology revolution has required pharmaceutical organizations to acquire key knowledge in molecular biology to conduct their R&D projects (MALERBA; ORSENIGO, 2001). In molecular biology, studies of the possible causes of the malfunctioning of the information transmitted by DNA gave rise to research into **genomics**, which analyzes genetic sequences to quantify the expression of genes in cells; **proteomics**, which involves experiments to identify the structure of proteins and their functions in living organisms; and **molecular dynamics,** which simulates the physical movements of atoms and molecules (OSTROWSKI; WYRWICZ, 2009).

Chiaroni, Chiesa & Frattini (2008) formulated a model, which we adopt in this study, to depict the typical R&D process that currently predominates in the pharmaceutical industry. Below we present a brief description of each step shown in Figure 1, as summarized by Oliveira (2011, p. 35-36). We have included additional references to deepen understanding of ideas developed in the steps of this model.

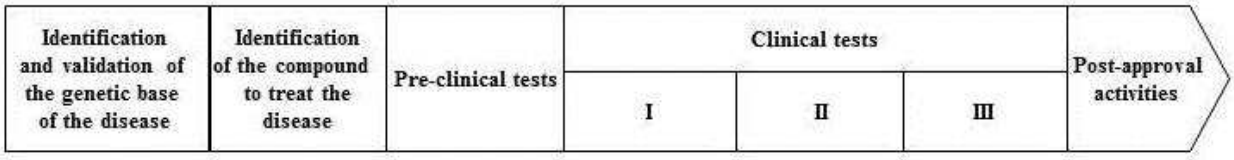

Figure 1 - R&D Process in the pharmaceutical industry
Source: Chiaroni et al. (2008).

The aim of the first step of the R&D process is to identify the gene, protein or sequence of both that lies at the base of the pathogen causing a target disease. The second step involves study of the gene or protein identified seeking to understand its interaction with the organism as a whole and to check, by accessing public databases, the possible existence of IP rights

over any substance used in the product targeted for development. A more detailed discussion of the techniques and tools applied in these initial phases can be found in Bare et al. (2010).

After evaluating the genetic base of the disease's evolution, it is necessary to identify a compound that has the desired effects in treating this disease. This compound is the active ingredient of the future drug. The optimization phase adds to this compound the other substances to be included in the drug formulation, aiming to protect, support and enhance the stability of the active ingredient and increase the patient's response to the medicine.

The pre-clinical tests investigate the effects, especially on animals (in vivo testing), of the mechanisms of absorption, distribution, metabolism, excretion and toxicity of the new drug. Before entering the clinical testing phases, it is necessary to obtain initial approval from the competent governmental agencies.

The clinical tests, with direct involvement of human patients, are carried out in three phases. In the first, the new drug is tested on a small group (20 to 80) of healthy people to assess its safety and determine the adequate dosage. In the second, the drug is tested on a larger group of people (100-300) affected by the disease of interest to evaluate the drug's effectiveness and determine the common short-term side effects and possible risks of its use. In the third phase, the sample of patients is enlarged (1000-3000) to confirm the drug's efficacy and assess the cost-benefit relation of its application. If these three phases are successful, the regulatory authority will approve the drug for sale.

The fifth and last step of the process entails the activities complementary to the purchase, production, logistics, marketing and sale of the new drug. It also involves post-marketing tests of the drug's performance throughout its life cycle, for the purpose of measuring additional risks and benefits.

Bastos (2005) presents more details of the pattern of technological innovation in the current pharmaceutical industry. An interesting discussion of the interdependence of the initial phases of scientific research and the other downstream activities of the innovation process in the pharmaceutical industry can be found in Malerba & Orsenigo (2001). Finally, the seminal article of Teece, Pisano & Shuen (1997) sheds more light on the importance of mastering the marketing steps to generate appropriate value in the creation of new drugs.

2.2 TECHNOLOGICAL COOPERATION NETWORKS

As pointed out by Oliveira (2011), establishing more open R&D structures is not a new argument, disconnected from the evolution of the capitalist economy during the twentieth

century. Since the rise of the systemic perspective in organizational theory, in the mid-1950s, different theoretical traditions have sought to understand the relationship of organizations with their external environment and the impact of this relationship on the innovation process (TROTT; HARTMMANN, 2009).

The image of the organization as a living organism in permanent interaction with its ecosystem has been explored in the organizational ecology literature (HANNAN; FREEMAN, 1977). The understanding that the firm is embedded in social relations with other organizations also contributed to shift the focus of analysis from the firm in isolation (UZZI, 1997). The constructs brought by embeddedness strongly influenced the vision of networks in various fields of study, especially strategy (DYER; SINGH, 1998; GULATI, 1998; JARRILLO, 1998). The construction of networks (GOMES-CASSERES, 1996) and establishment of strategic alliances (NOOTEBOON, 1999) started to be seen as effective mechanisms for access to external sources of knowledge that could be applied in the innovation process.

From the perspective of distributed capabilities (COOMBS; METCALFE, 2000), networks use organizational routines that allow each partner to complement the knowledge necessary to generate and disseminate new products and processes, using purposeful specialization and multidirectional flows to transfer knowledge between partners. According to Dantas & Bell (2009, p. 831), learning and innovation networks (LIN) are "[...] organizational arrangements that involve actors with different capabilities and that are concerned with knowledge flows and the coordination of learning and innovation."

As pointed out by Laursen & Salater (2006), recognition of the importance of external ties for firms' innovative performance does not mean the absence of factors that condition the effectiveness of collaborative networks. This results from the cognitive difficulty of dealing with an excessive number of partners and technological paths. In line with this argumentation, Pisano & Verganti (2008) state that the type of collaboration with external partners depends on the maturity of the knowledge sought.

Figure 2 describes the typology proposed by Pisano & Verganti (2008), which we adopt in this study. Then we present a brief description of the objectives and mechanisms that enable each type of collaboration of the model, as presented by the authors of the original article and summarized in Oliveira (2011, p. 38-40). This model involves aspects of governance and the degree of openness of the cooperation networks, discussed in more detail by other authors associated with the economics of innovation and management of innovation.

We add new references to allow the reader to delve more deeply into the ideas in question.

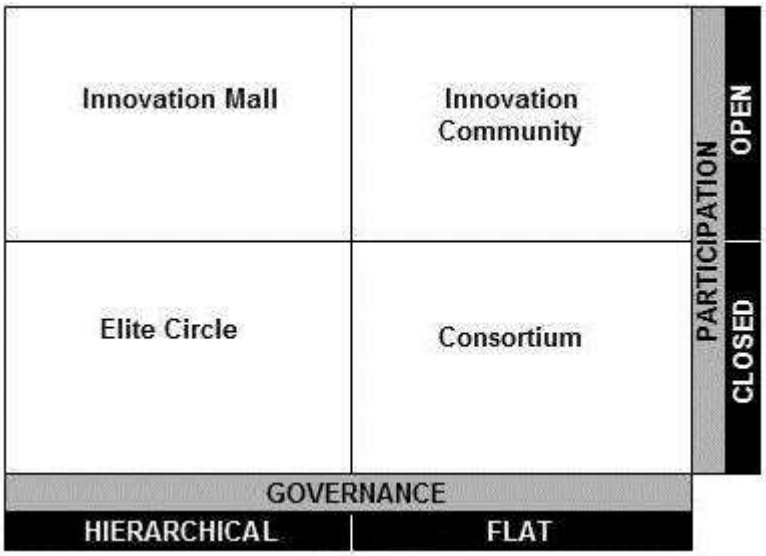

Figure 2 – Modes of collaboration with external partners
Source: Pisano & Verganti (2008).

In the **innovation mall**, the company receives a large number of solutions regarding scientific domains that can go beyond its knowledge or experience, but it still wants to maintain control over the direction of the innovation process. This mode is recommended when the company detains the key knowledge and wants to maintain the integrity of a system, using the network to accelerate the development of less complex incremental innovations. For more details about the types of incremental or radical innovation, see Sivadas & Dwyer (2000). The biggest challenge is to attract many ideas from various fields of knowledge, examine them systematically and choose the most suitable direction. Huston & Sakkab (2006) discuss the impact of R&D resulting from connection to technology markets. The mechanisms that enable this mode are: i) the ability to understand the needs of customers and to test and examine solutions at acceptable costs (a summary of experimentation processes can be found in Thomke [2003]); ii) the capacity to design systems that break down large problems into discrete parts so that each partner can work autonomously, for subsequent integration by the company; and iii) the use of information platforms that facilitate dynamic collaboration. Pitassi (2012) contains a deeper discussion of virtual collaboration networks.

In the **innovation community**, usually associated with open source code movements, any company or partner can propose problems or offer specific solutions with a well-defined outline. The interaction between joining open code communities and following competitive or open technology strategies is covered in Chesbrough & Appleyard (2007). This mode is recommended when the firm can use the knowledge generated in the network to improve its

own products and processes. The greatest challenge is to create value with the knowledge exchanged in the network to a greater extent than the value that would be created by keeping the knowledge within the company (PITASSI, 2012). Its mechanisms are: i) a modular product or service architecture that facilitates delineation of the problem and development of solutions (the relationship between modular architecture and competitive strategy is treated in more detail in Christensen [2006]); ii) incentives that foster greater density of the community vis-à-vis competing technologies; and iii) Internet portals that allow participation of the partners (see PITASSI, 2012).

In the **elite circle,** the company selects the partners it considers most qualified in the knowledge areas underlying the intended solution, while maintaining strict control over the evolution of the research and the capture of value from the innovation. It is recommended in moments of radical innovation (see SIVADAS; DWYER, 2000) or the initial phases of research, when the correct direction is not yet clear. The biggest challenges are to identify the fields of underlying knowledge and the most qualified partners and to choose the correct direction. Laursen & Salter (2006) analyze the impacts of the amplitude and depth of external relationships on the effectiveness of collaboration networks.

The mechanisms that enable this mode are the abilities: i) to identify a customer need not yet satisfied (Brown [2008] highlights the contribution of thinking inspired by design for customer-oriented innovation); ii) to identify partners that have the talent to conceive the solution; iii) to establish relationships of trust and incentive mechanisms that favor the most qualified partners and remunerate the specific investments (the seminal article of Dyer & Singh [1998] explains the contribution of the constructs associated with the relational view to strengthening the ability to maintain effective ties with external partners); iv) to develop a product architecture that facilitates interactions and the subsequent developments; and v) to virtualize the steps of the innovation process by means of ICTs (DOGSON et al., 2006).

In the **consortium,** no one firm alone masters all the fields of knowledge potentially involved in the solution. Mutual dependence and multiple directions of knowledge exchange discourage attempts at control over capture of the value generated by the innovation (this is one of the central arguments in favor of adopting an open innovation strategy in the vision of Chesbrough [2006]). It is recommended in situations where research involves high costs and risks, so all partners can divide the costs and rewards of the particular innovation. The greatest challenges are to identify the underlying knowledge and the partners that are best qualified and to influence the direction of innovation to obtain contributions that will be profitable for

the company (the article of LICHTENTHALER; LICHTENTHALER [2009] contains an interesting discussion of this ability). The mechanisms that enable this mode are: i) the ability to find partners with the knowledge necessary and capability to work with distributed and complementary knowledge (this capability is discussed in COOBS; METCALFE [2000]); ii) the establishment of processes and rules that stimulate the partners to work in concert to attain shared objectives; and iii) the adoption of ICTs that permit remote development, simulations and virtual prototyping (see THOMKE, 2003).

2.3 THE USE OF ICTS IN SCIENTIFIC EXPERIMENTS IN THE PHARMACEUTICAL INDUSTRY

With the advances in digital technology, ICTs have become tools to support management of R&D, allowing people, as argued by Dogson et al. (2006, p. 335), to "experiment with different futures". Thus, the way that firms generate idea, conduct experiments, test and prototype new products, services and business processes can be altered by ICTs (THOMKE, 2003), particularly in a context in which R&D is increasingly undertaken with open relational models (CHESBROUGH, 2003), supported by use of virtual teams (GASSMANN; VON ZEDTWITZ, 2003).

In the case of pharmaceutical organizations, the consolidation of molecular biology as an alternative route for development of biopharmaceuticals has brought a recurring need to analyze a growing volume of data regarding genetic maps and protein structures. The respective experiments involve various areas of knowledge and require manipulating large volumes of data (BALDI; BRUNAK, 2001; WAGNER, 2006). The resulting complexity has led to the development of bioinformatics, a field of knowledge that has become established in recent decades as a result of the interdependence between the evolution of ICTs and molecular biology (ATTWOOD et al., 2011). Bioinformatics experiments involve the interplay of knowledge from computer science, information science, mathematics, physics, chemistry and biology, among others (WAGNER, 2006).

The improvement of computational infrastructure has particularly facilitated molecular biology experiments, through the use of database management systems (DBMSs), scientific workflow management systems (SWFMSs), laboratory information management systems (LIMSs) and 2D and 3D graphic platforms for visualization of molecules. Bioinformatics and computational biology allow solving complex biological problems, such as genetic sequencing, analysis of gene expression, determination of protein structures and inference about phylogenetic trees (BALDI; BRUNAK, 2001; SETÚBAL; MEIDANIS, 1997).

For these purposes, the Internet is a fundamental tool, not only in the process of dissemination and sharing of the results generated and stored in biological databases, but also for remote processing of genomic data spread among various sites on the World Wide Web (WWW) (LESK, 2008). Table 1 summarizes the types of ICTs identified in the literature on technological innovation.

Table 1 – Use of ICTs in Technological Cooperation Networks

ICTs	Objective	Bibliographical References
Workflow management systems to support scientific experiments	To manage the sharing of data, ideas and results of experiments among internal and external researchers.	Digiampietri (2007); Curcin & Ghanem (2009); Hacievliyagil (2007).
Knowledge management systems	To identify, create, present and share knowledge in the context of health organizations.	Bose (2003); Barbosa et al. (2009); Febles Rodriguez & Gonzalez Perez (2002); Huston & Sakkab (2006); Rothwell (1994); Nambisam (2002).
Grid information technology	To coordinate the use of distributed computational resources in multi-organizational scientific experiments.	Maqueira & Bruque (2007); Neubauer, Hoheisel & Geiler (2006); Digiampietri (2007).
Computational systems for experimentation	To support genomic and proteomic experiments involving manipulation of large amounts of data and interactions in short time periods and three-dimensional modeling of biomolecules	Catanho et al. (2007); Dogson et al. (2006); Sakkab (2002); Lenoir (1998); Naznin et al. (2011); Thurow et al. (2004).
High throughput screening	To accelerate the discovery of drugs by means of the association of sophisticated computer programs for control, robotics, optics, instruments for manipulation of liquids and visualization.	Chen (2006); Bleicher et al. (2003); Persidis (1998).
Tele-interaction	To enable the exchange of information, provision of services and interaction of virtual teams of researcher, to overcome barriers of time and space.	Hebert et al. (2006)
Virtual prototyping, simulation and optimization	To create virtual prototypes, products and productive processes.	Catanho et al. (2007); Bare et al. (2010); Dogson et al. (2004); Kohlbacher et al. (2007), Lenoir (1998); Thomke (2003).
Toolkits for clients	To offer user-friendly IT tools to clients and partners to enable them to participate in the development of new products.	Nambisan (2002); Von Hippel & Katz (2002); Freeman & Soete, (1997)
Web tools for virtual collaboration	To use blogs, wikis and virtual communities, including open source, in collaboration in R&D.	Brown (2003); Gassman & Von Zedwitz (2003); Pisano & Verganti (2008); Stajich & Lapp (2006); Trieglaff & Sturm (2007).
Company portals with functionalities to support innovation	To use companies' portals on the Internet as a means to regulate the connection with potential inventors and researchers.	Sakkab (2002); Pisano & Verganti (2008).

Virtual knowledge brokers	To use infomediaries to leverage access to the information available in the global technology market.	Hacievliyagil (2007); Verona et al. (2006).
Laboratory information management systems	To manage, optimize and automate laboratory processes.	Nakagawa, 1994; Thurow et al., (2004)

Source: Prepared by the authors.

3 METHODOLOGY

The survey described in this article sought to understand, in the opinion of the scientists who work in the R&D areas, the contribution of ICTs to the technological collaboration projects of pharmaceutical organizations, which explains the choice of a qualitative approach (DENZIN; LINCOLN, 2000).

The primary unit of analysis (YIN, 1994) was the technological collaboration projects of Bio-Manguinhos indicated by the office of the vice-presidency for technological development. This study is both descriptive (VERGARA, 2007), with the purpose of identifying the types of ICTs used, and explanatory, because we discuss how these ICTs are used in the projects and their contribution to the intended objectives.

With respect to the means, this is a single case study. The use of single case studies is appropriate in emblematic cases (YIN, 1994; STAKE, 1995). We chose Bio-Manguinhos because it is considered a benchmark in Brazil in the production of vaccines and diagnostic kits, and it has relied heavily in recent years on cooperation with other entities to accelerate its technological innovation.

The research subjects were 14 scientists involved in the R&D area: the vice-director of the technological development area, responsible for the R&D center; project managers; program managers; the project office manager; IT manager; information security manager; and manager of the Laboratory for Monoclonal Antibody Technology (LATAM).

Besides the interviews, we gathered data from published articles and organizational documents. The interviews were conducted between April 2011 and March 2012. Personal observation of participants is seen as an essential source of data (CHECKLAND, 1991). In this case, one of the authors is the manager of the IT area of Bio-Manguinhos, with first-hand familiarity with the IT projects in support of the R&D area. The interviews were supported by a script and were recorded with the prior authorization of the respondents. The data collected were treated by applying categorical content analysis (BARDIN, 1979).

4 PRESENTATION AND DISCUSSION OF THE RESULTS

We directly studied seven R&D projects carried out in collaboration with partners: 1) nucleic acid test kit, called NAT HIV/HCV kit, developed by the reagents program; 2) dengue vaccine, of the viral vaccines program; 3) microarray, of the reagents program; 4) yellow fever vaccine, of the viral vaccines program; and 5) three rapid tests, involving three projects: 5.1) test to confirm HIV (rapid immunoblot test); 5.2) rapid test for syphilis; and 5.3) rapid test for canine visceral leishmaniasis. The consolidated results of the survey can be seen in Tables 2 and 3. The discussion that follows is focused on the aspects we believe are most relevant to respond to the research question and to meet the aims of this article.

Table 2 – Consolidated Results of the Interviews – Part 1

Project	Objective	Respondent	Partner	Steps of the R&D Process			Mode of Collaboration with Partners
				Start	Current Moment	Focus	
1) NAT	To develop a technology (real-time PCR) based on molecular biology to identify more than one pathogen (HIV and HCV) at the same time (multicentric) with the same reaction – diagnostic kit.	2) NAT project manager (PhD in biology from UFRJ, with specialization in genetics)	1) UFRJ (Rio de Janeiro) 2) IBMP (Curitiba) 3) PerkinElmer (USA) 4) Qiagen (Germany) 5) Applied (USA)	Identification and validation of the genetic base	Post-approval activities (last step)	Post-approval activities (last step)	Elite Circle
2) Dengue	To develop a vaccine to prevent dengue, where the adjuvant is the intellectual property of the partner (industrial secret).	3) Project manager (PhD in biology from IOC, with specialization in virology) 4) Assistant to the vice-director for technological development (PhD in Economics from COPPE/UFRJ, with specialization in production engineering)	GSK (Belgium)	Pre-clinical tests	Pre-clinical tests	Post-approval activities	Elite Circle
3) Microarray	To develop a multi-test for serological sorting of all blood donated in the country by creating a new technology denominated XMAP, to replace the current technology called ELISA.	5) Micro-arrangement project director (MSc in cellular biology from IOC, with specialization in industrial management of immunobiological substances)	1) IBMP (Curitiba) 2) ICC (Curitiba) 3) Partner "X"	Pre-development	Experimental development	Post-marketing (last step)	Elite Circle
4) Yellow fever	To develop a new vaccine for yellow fever (based on expression in plants) that no longer has the serious risks of the current vaccine which is an attenuated vaccine, with live and attenuated virus.	6) Manager of the Program for Viral Vaccines and manager of the Yellow Fever Project (PhD in biology from UFRJ, with specialization in biological chemistry)	1) Fraunhofer (USA) 2) Ibio (USA)	Identification and validation of the genetic base	Pre-clinical tests	Post-approval activities (last step)	Elite Circle
5) Test to confirm HIV (immunoblot)	To develop a test to confirm diagnosis of HIV.	7) Manager of the Rapid Testing Technology Transfer Projects (MSc in microbiology/immunology from IOC, with specialization in cellular and molecular biology)	Chembio Diagnostics (USA)	Pre-development	Post-marketing	Post-marketing	Elite Circle
6) Rapid tests for syphilis	Simple transfer of technology of a rapid test for syphilis.			Product registration (simple technol. transfer)	Post-marketing	Post-marketing	
7) Rapid tests for canine visceral leishmaniasis	To develop a new technological base for a rapid test for canine visceral leishmaniasis, to replace the old confirmatory test that uses immunofluorescence technology.			Pre-development	Post-marketing	Post-marketing	

Table 3 – Consolidated Results of the Interviews – Part 2

Type of ICT				
Some of the ICTs used in the projects	**Limitation if the ICT were not available**	**ITC desired by the R&D team**	**Contribution of the desired ITC**	**Classification of the ITC used in the collaboration strategy**
1) Automatic sequencer with a sequencing analysis system; 2) Real-time PCR with a system to interpret data and generate results; 3) Automation of pipetting; 4) Technology to extract nucleic acid; 5) High throughput screening; 6) PubMed portal; 7) GenBank sequences bank; 8) Teleconference.	Delay of the process	1) Videoconference tool in the premises of Bio-Manguinhos; 2) System to store and exchange data with partners.	Agile consultation of information.	1) Web tools for virtual collaboration; 2) Computational systems for experimentation; 3) Virtual participation and visualization; 4) Tele-interaction; 5) High throughput screening; 6) Laboratory information management system; 7) Virtual knowledge brokers; 8) Portal of the company with functionalities to support innovation.
1) Teleconference; 2) PubMed portal; 3) GenBank sequences bank; 4) Genomic sequencing; 5) Analysis of sequencing; 6) Encrypted email; 7) System to record meeting minutes, data and results of analyses (of the partner); 8) Gotomeeting for videoconference (of the partner)	Delay of the process	1) LIMS integrated with EPM; 2) Use of SharePoint for exchange with external partners.	1) Avoids the need for travel to branch of partner; 2) Retention and sharing of information.	1) Web tools for virtual collaboration; 2) Computational systems for experimentation; 3) Virtual participation and visualization; 4) Tele-interaction; 5) Laboratory information management system; 6) Virtual knowledge brokers; 7) Portal of the company with functionalities to support innovation.
1) xMAP technology; 2) PubMed portal; 3) xPONENT system or similar for reading and generation of a CSV file with results of the tests conducted; 4) Automation of the pipetting process; 5) EPM; 6) Teleconference.	Delay of the process	1) System to record lessons learned; 2) Knowledge management system.	1) Retention and dissemination of knowledge; 2) Velocity of the process.	1) Web tools for virtual collaboration; 2) Tele-interaction; 3) Laboratory information management system.
1) Agro-infiltration technology; 2) Sequencing; 3) Sequence analysis; 4) High throughput screening; 5) PubMed portal; 6) GenBank sequences bank; 7) Teleconference; 8) EPM.	Delay of the process	1) 1) Videoconference tool in the premises of Bio-Manguinhos; 2) Knowledge management system; 3) System to record lessons learned.	1) Facility of communication with partners; 2) Velocity of interaction in the process; 3) Retention and dissemination of information.	1) Web tools for virtual collaboration; 2) Computational systems for experimentation; 3) Virtual participation and visualization; 4) Tele-interaction; 5) High throughput screening; 6) Laboratory information management system; 7) Virtual knowledge brokers; 8) Portal of the company with functionalities to support innovation.

1) Lateral flow immunochromatography in a dual path platform (DPP) technology; 2) PubMed portal; 3) Teleconference; 4) Videoconference; 5) Skype and MSN; 6) EPM.	Delay of the process	1) FTP channel to exchange files with partners; 2) System to manage knowledge based on lessons learned; 3) EPM (with SharePoint) available to the partner on the web; 4) System to exchange information with external partners via the web; 5) Videoconference tool in the premises of Bio-Manguinhos.	1) Agility; 2) Security; 3) Fast access to information.	1) Web tools for virtual collaboration; 2) Tele-interaction; 3) Laboratory information management system.

The results show that Bio-Manguinhos makes a careful effort to choose partners to participate in the technological cooperation projects involved in the initial phases of the R&D process. The option for the "elite circle" collaboration mode, predominant in this state, is in agreement with the model proposed by Pisano & Verganti (2008). However, even after acquiring the know-how, Bio-Manguinhos maintains the ties with the partners based on the belief that this option will accelerate the R&D process.

The evidence indicates that this option can be associated with the desire to speed up the R&D process, considering that the main acquisitions of raw materials, technologies and other inputs can be carried out directly by the partner, without the need to overcome the bureaucratic hurdles to which public-sector research organizations are subject in Brazil. The following comment reveals this concern:

> I think that Bio-Manguinhos practices an elite circle... the inputs and raw materials can be purchased by the partner, enabling use to accelerate the process.

With respect to the ICTs identified in the literature examined, **tele-interaction** was present in all the technological collaboration projects studied, particularly those involving partners located outside of Brazil. Up to the date of the interviews, the teams of Bio-Manguinhos basically used teleconferences. As can be seen in the following report, the unavailability of videoconference technology within Bio-Manguinhos caused negative impacts:

> In particular, I have not had the opportunity to use videoconferences, but teleconferences were not very successful, because, as I said, I prefer to see instead of just hear the person with whom I'm exchanging ideas, because I can read the facial expressions.

In the absence of videoconference technology, some of the managers interviewed said they use MSN and Skype through their personal computers to exchange information, since the information security rules do not allow installing these programs in the organization's hardware. By resorting to this alternative, information recognized by the respondents themselves as confidential might be vulnerable. The alternative use of the communication platforms of partners causes inconveniences, as can be noted from the following comment:

> If we could have videoconferences here in Bio-Manguinhos, our process would go faster. For you to have an idea, when we needed to hold a videoconference with GSK, we had to go to Jacarepaguá to use their room and equipment, and this took a lot of time.

At the time of the interviews, Bio-Manguinhos did not have any information system (IS) to support the recording and sharing of the information generated during the R&D process with external partners. This lack caused the managers to resort to a Windows folder

called “Restricted” for this purpose. Even though the respondents alleged this folder served its objectives, the study showed that they also acknowledge that the ideal situation would be to have an IS applied to **knowledge management,** as reflected in the following comment:

> Today we’ve learned a lot from exchanging internal information and have learned from experiments and from the errors of our colleagues, but we aren’t that near to all the projects, so we haven’t had an opportunity for internal exchange with all the program managers. If we had a database of knowledge and lessons learned it would be a dream come true.

It is important to point out that at the time of the survey Bio-Manguinhos had an ICT that could satisfactorily serve this function, the SharePoint software from Microsoft, a collaboration tool that is part of the Enterprise Project Management software package (EPM) acquired by the organization. EPM integrates a library of documents that, by means of SharePoint, can be shared over the web with external partners. To circumvent the limitation indicated by the above respondent, some project managers, repeating the practice already observed with other tools, said they used the SharePoint of external partners. This use considerably streamlined the exchange of information, and hence the speed of the project, as can be seen from the narrative below.

Even though acknowledging that the gains were only partial, the vice-director of the Technical Development area (TD) argued that it was necessary to change the internal culture of Bio-Manguinhos to create a solid and reliable base to permit use of SharePoint as a knowledge management tool for the projects conducted in collaboration with external partners:

> In reality, people have adhered to and embraced this idea, of making this available to the project managers, program managers, external partners.... In the final analysis, we need to create this culture and use this tool better.

This narrative corroborates the evidence found in the literature that it is not sufficient just to adopt an ICT for it to work properly. It has to be implemented adequately, and organizational mechanisms must be created that stimulate people to capture the potential benefits of these technologies (KLEIN; SORRA, 1996).

Bio-Manguinhos used, when applicable, **high throughput screening** (HTS) technologies in the R&D projects studied. In the yellow fever project, for example, this technology was used in the process of formulating the vaccine, when simultaneous tests of various substances were conducted at high speed to know which of them would best allow stabilizing the target protein. HTS was also used in the NAT project, which operated 24 hours a day, to enable analysis of 552 samples in just seven and a half hours.

The evidence gathered demonstrated that the **virtual collaboration web tool** was also used in all the projects studied. Researchers often searched the PubMed portal to find bibliographical material, such as scientific articles, relevant to the projects under way in the organization. Among the advantageous uses of this tool, the following were mentioned: i) to discover if a project similar one being conducted by Bio-Manguinhos existed; ii) to carry out patent searches; iii) to find companies able to produce inputs relevant to projects; and iv) to learn the results of experiments carried out by other researchers that might contribute to the R&D projects of Bio-Manguinhos.

The R&D area of Bio-Manguinhos relies intensively on this ICT to consult the cell sequence database called the GenBank, present at the PubMed portal. By means of this module, the researchers search for sequences that can be sent to specialized companies (contract research organizations - CROs), to engage them to synthesize and supply primers for genetic sequencing to the R&D team. Besides downloading the sequences, the researchers upload to the GenBank the sequences discovered internally or by other molecular biology partner laboratories.

The evidence obtained shows that **computational systems for experimentation** were used in the yellow fever, dengue and NAT projects. In these efforts, this ICT was applied for viral sequencing and also to compare the sequences generated by the internal R&D team and those synthesized by specialized firms, like CROs. However, in the case of genome sequencing, which requires more complex computer processing, due to the lack of adequate infrastructure, Bio-Manguinhos resorted to other platforms of FIOCRUZ, and in some cases, outside the FIOCRUZ campus.

Virtual prototyping and visualization also were used by Bio-Manguinhos at the time of the survey. For example, the R&D team of the yellow fever project visualized and analyzed the three-dimensional structures of the protein of the virus by using a specific tool for sequence analysis containing complex mathematical algorithms. Another example was the dengue project, which used this ICT to analyze the sequences by phylogeny. To carry out these analyses, Bio-Manguinhos used specific free computer programs, some available from websites (such as www.nvbi.nlm.nih.gov). These programs allowed uploading a sequence defined by the researcher to a database of the provider for remote processing.

At the time this study was carried out, the LATAM of Bio-Manguinhos was developing monoclonal and polyclonal antibodies to meet the needs of internal and external researchers. These biological materials were stored in a biological material bank (BMB), managed by

LATAM. To meet the laboratory's needs, the internal IT team, with support from the Institute of Engineering of Rio de Janeiro Federal University (COPPE/UFRJ), developed a specific **laboratory information management system (LIMS)**. This system, implemented about three years beforehand, allows users to record the movement of antibodies and cells in the BMB, thus assuring total traceability of these biological materials, which enables identification of: i) the physical storage place (pressurized bottle, canister, rack, cryotubes); and ii) the origin of the demand and the name of the project for which the they are used.

Recognizing the importance of the knowledge provided by the IT area, the respondents stated that other modules would be implemented to expand the scope of the system. The TD (technological development) area also intends to integrate it with the project management software (EPM) to allow researchers to plan the use of biological materials related to the activities of projects.

When the R&D projects analyzed here required more complex genome sequencing, Bio-Manguinhos employed the molecular biology platforms at its disposal, such as those of the Laboratory for Computational and Systemic Biology (LBCS) of Oswaldo Cruz Institute (FIOCRUZ) in Rio de Janeiro, the Molecular Biology Institute of Paraná (IBMP), the Renê Rachou Research Center, belonging to FIOCRUZ in the state of Minas Gerais, and the National Laboratory for Scientific Computation (LNCC), linked to the Ministry of Science and Technology.

To have access to these laboratories, Bio-Manguinhos signed "letters of commitment" with them, a type of contract between governmental entities that authorizes the transfer of public funds. As reported in several of the interviews, and subsequently ratified by the vice-director for DT, Bio-Manguinhos did not internally carry out more complex genome sequencing experiments, based on a policy that this was not its focus. If this reality were to change, the vice-director expressed the belief that it would not be necessary to create a bioinformatics laboratory, since the organization could opt to form a partnership with a specialized laboratory.

Finally, this study's results indicate that significant gains could be obtained with greater approximation between the IT and R&D areas, even through simple initiatives. It is interesting to note that at the time Bio-Manguinhos already had basic technologies, like File Transfer Protocol (FTP) and even Virtual Network Communities (VNCs), to overcome communication and security problems. In response to the opinions expressed in the interviews, particularly those from the technological development area, the IT area made

available a FTP to facilitate the transfer of files related to R&D projects with outside partners. The development of the LIMS for the LATAM is an emblematic example of how the best practices of information management, theoretically the main domain of IS professionals, can contribute to the R&D area of Bio-Manguinhos.

The case study brought evidence that the still predominant culture among the molecular biology researchers, especially those engaged in bioinformatics, favors the use of open code tools and public Internet portals. Given the difficulties usually found in organizations regarding support for corporate IT initiatives, these professionals resort to Office tools to conduct their analyses. The comments collected show that these tools have assumed a role in Bio-Manguinhos that is not the most suitable in the context of molecular biology research laboratories, which can benefit from more robust tools that are integrated with the other clinical research and medical informatics systems, inside and outside the organization. It can be affirmed that this situation is partly due to the lack of knowledge exhibited by the researchers about the potential contribution of corporate ICTs.

5 CONCLUSION

The objective of this article was to identify and discuss the contribution of ICTs to the technological cooperation projects of Bio-Manguinhos. The results of the study show that the partnerships established by the organization contributed decisively to accelerate the projects analyzed, overcoming to some extent the restrictions imposed on public R&D centers in Brazil. The preferential adoption of the “elite circle” mode to get around these constraints, in circumstances that would justify the substitution of this mode by other more flexible modes of collaboration, can be associated with the still predominant concern within the organization regarding control of IP.

The shortage of projects involving interdependent collaboration, with two-way flows of knowledge, appears to explain why some of the ICTs identified in the academic literature on bioinformatics, such as scientific workflow and Git, were not yet used by Bio-Manguinhos at the time of the interviews. Therefore, a change in direction toward consortiums could alter the organization’s perception of the value of these ICTs. This supposition can be addressed in a future study: If Bio-Manguinhos becomes deeply involved in processes for co-development of drugs or vaccines, what would be the contribution of the ICTs currently absent to the organization’s innovative capability?

The study also showed that Bio-Manguinhos does not have a structured knowledge management system, posing serious limitations on the interaction of the internal R&D teams

and their interaction with the R&D teams of technological partners. Given that Bio-Manguinhos currently has a large contingent of outsourced staff, and in face of the difficulty of retaining talents in the context of public research organizations, the absence of this ICT increases the risk of losing valuable knowledge. To rectify this absence, researchers typically resort to tools of the Office platform, which are inadequate to deal with the complexities of technological innovation indicated in the literature.

We believe this study makes relevant contributions to administrative theory and practice. In theoretical terms, the study expands the existing knowledge by demonstrating the relevance of deeper research into the use of ICTs to support management of technological collaboration in highly complex organizational contexts, as is the case of pharmaceutical companies. From the practical standpoint of management of science, technology and innovation (CT&I), the study allows managers of R&D projects that involve biotechnology, especially those associated with Brazilian public-sector pharmaceutical organizations, to make more effective use of the available ICTs.

The study brings further evidence that molecular biology has become an area of knowledge that relies heavily on information technologies, so closer approximation between the two fields is important. Because of the nature of the R&D processes in the pharmaceutical industry, great benefits can be gained from more thorough integration between the corporate R&D and IT areas, particularly if the organization in question has its own bioinformatics or computational biology area. The results also make it clear that the rules on access to and security of information of the R&D area should not be the same as those for the other areas of the organization.

In closing, we believe that in a scenario of growing use of cloud computing, web services and software as a service (SaaS), the contribution of a company's IT area should be increasingly directed to its specific business objectives. The results of this case study reveal that if the IT area is suffocated by administrative demands with transnational character, leaving insufficient time and inadequate training to explore the reality of the typical processes of the R&D area, this can seriously impair the ability to innovate in organizations involved in the life sciences.

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