The evolutionary nature of innovation in the health sector in developing countries: an analysis of the university-organisations collaboration in Rio Grande do Sul[1], Brazil

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Abstract

Following the innovation systems approach, this paper's goal is to analyse the interactions established between universities - as to their research groups - and other organisations - in particular hospitals, but also industrial firms - focusing on the development of products and/or processes that are innovative for the human health, as well as on advances in medical services. Thus, this paper aims to contribute to the characterisation of processes that generate knowledge and innovation in the health sector in emerging countries, such as Brazil. In order to do so, the interactions of five research groups from the Federal University of Rio Grande do Sul (UFRGS) were analysed. In addition to the field research conducted with these investigated groups, through in-depth interviews, the study was based on secondary data collected from the Directory of Research Groups of the National Council for Scientific and Technological Development (CNPq). This exploratory study identified important characteristics of the interactions established between the involved actors and seeks advances in medical care and in innovation development: multidisciplinary researcher teams qualify the process of generating knowledge and innovations; the teaching hospital is the key actor; patients are relevant actors in the establishment of interactions and generation of knowledge by the groups, whereas clinical research constitutes an important way of creating new ideas; other researchers from research centres or universities in Brazil and abroad participate in the process of generating knowledge; disconnection between scientific and technological production, since the investigated groups have high scientific production and very low interaction with the manufacturing industry. These characteristics corroborate at large other findings that have been already published in specialised literature.

Key words: Health Innovation System; university-organisations collaboration; university hospitals; interaction networks; Brazil.

1. Introduction

Several characteristics regarding innovation in the healthcare system became central objects of research within the innovation systems approach. The increasing technological content associated with pharmaceuticals and both medical machinery and equipment; the interdisciplinary character associated with knowledge in this area; the importance of medical and hospital services as proactive agents of innovation; and the new and increasing demands related to the tendency of population ageing are some of the reasons that give prominence to the health sector within the studies on innovation and public policies.

As to the importance of medical and hospital services, recent academic papers point to the necessity of addressing the interrelationship between industry and services in order to approach innovation in health care. These studies show in particular further research on hospitals as selection and innovation-generating environments.

Based on the theoretical framework of innovation systems and the context of technical change in the health system, the question that this paper aims to answer is: *Which features are presented in the interactions between universities and other organisations with regard to knowledge generation and innovation in medical assistance, products and/or processes in the health sector?*

[1] Rio Grande do Sul (RS) is the state situated in the extreme south of Brazil.

Our goal is therefore to analyse the interactions established between universities — as to their research groups — and other organisations[2] — particularly hospitals, but also industrial firms — focusing on the development of products and/or processes that are innovative for the human health, as well as on advances in medical services. Thus, this paper aims to contribute to the characterisation of processes that generate knowledge and innovation in the health sector in emerging countries such as Brazil.

In order to perform this study, the case-study methodology was chosen to examine research groups that perform interactions with other organisations (hospitals, companies, etc.) over time. This method is justified by the necessity to analyse information qualitatively. The interactions from five research groups of the Federal University of Rio Grande do Sul (UFRGS) were examined. These groups were selected based both on the data gathered from the Research Groups Directory (DGP) of the National Counsel of Technological and Scientific Development (CNPq) and on the results presented by the work of Tatsch, Ruffoni and Botelho (2016), which identify the research groups from UFRGS active in the health services that establish the largest number of interactions with organisations *lato sensu*. In-depth interviews with the leaders of these groups were conducted with basis on a questionnaire. In the face of these methodological procedures, this study can be characterised as exploratory.

This paper's central contribution is to present the interactions established by research groups of academic excellence in the health field, in order to generate knowledge and innovation, especially interactions with hospitals. It is important to stress that the groups selected for the investigation belong to UFRGS, a traditional public university and important actor for the Brazilian innovation and knowledge system. Due to its interactions, UFRGS has already been pointed out as a gatekeeper (Costa; Ruffoni; Puffal, 2011).

The article is divided into four sections in addition to this introduction. In the second part, the theoretical framework that supports this study is explained briefly. In the following section, methodological procedures are described; and subsequently, the results of the empirical research are discussed. The final considerations are to be found in the last part of this paper.

2. Theoretical Framework

Neoschumpeterian literature conceives innovation as a systemic phenomenon that originates essentially from the various interactions that organisations establish in the environment in which they operate.

The recent advances in this literature led to the construction of the innovation systems approach in its various areas of analysis: national innovation systems (Edquist, 2006; Freeman, 1995; Lundvall, 1988; 1992; Nelson, 1993), regional innovation systems (Cooke, 1998; Asheim; Gertler, 2006) and sectoral innovation systems (Malerba, 2002).

Considering these points of view, the analysis of how the interactions that produce knowledge and innovation develop themselves is central. Interactions established with suppliers, competitors, clients, public and private agencies of promotion and support, universities and research centres are considered, since they rank among the most important agents (Lundvall, 1988; 1992).

Mowery and Sampat (2006, p. 221), in summarising the results of these various approaches, indicate that "[...] research collaboration between universities and industry is growing throughout the industrial economies, in university systems with very different structures".

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[2] It is important to point out that the term “university–industry”, commonly used in the literature, will here be replaced by “university-organisations”, based on the fact that, given its multiple and distinctive interactions, the health sector demands a broader approach. A further reason to make use of this term relies on the meaning assigned to "company" in the database consulted for the gathering of secondary data: it is not used *stricto sensu* as "firm", but as "organisations in a general way", such as universities, city government units, associations, hospitals, and other research groups.

These interactions tend to present a strong sectoral content, considering Pavitt's (1984) pioneer propositions. Thus, the productive sectors differ in relation to the types of interactions they establish, as well as to the actors involved in these knowledge and information exchanges.

In science-intensive sectors, interactions between companies and universities and/or research centres are fundamental. This is the focus of several recent works that, within the innovation systems approach, lead to the study of the relationships between universities and research centres and companies, assuming that these relationships are increasingly important in modern economies. Knowledge inputs, regarding both scale and diversity aspects, as well as the interdisciplinarity and collaboration between numerous actors, at a national or international level, are fundamental requirements for scientific research and innovation.

The pharmaceutical industry and a considerable part of the machinery and equipment industry that supplies health services play an important role in science-intensive fields of scientific knowledge. These industries often interact with hospitals, especially with university hospitals, *loci* of prominent research in the medical field. Several learning and knowledge flows circulate from university hospitals to the industry and vice versa, performing reciprocal interchanges (bidirectional flows), in which the complexity of the interactions and of the non-deterministic changes throughout the process of developing new technological solutions (Dosi, 1982) constitute an eminently evolutionary process (Nelson; Winter, 1982; Nelson *et al*., 2011).

With regard to the evolutionary nature of research and medical innovation, Gelijns and Rosenberg (1995) describe the inadequacy of the linear model of innovation as a theoretical approach to this area of knowledge. They also highlight the great complexity behind technological change in medical products and services and, therefore, point to the necessity of taking the various types of interactions that support the innovative process into consideration. Consoli and Mina (2009) argue that the activities are strongly influenced by organisational, strategic and relational factors, which differ from the archetypes of product or process innovation.

Based on specific developments in this field and using different methodological approaches, several studies point to the evolutionary nature of research and innovation in the health sector. This is the case of Metcalfe, James and Mina (2005), who discuss the development of intraocular lenses for cataract treatments in the ophthalmological field. Still in this field, treatments for glaucoma and coronary diseases are discussed by Consoli and Mina (2009) from the evolutionary approach.

These and other works devote particular attention to medical services as crucial agents in the innovative process. A specific type of user-producer relationship (Lundvall, 1988; Hicks; Katz, 1996; Albuquerque; Cassiolato, 2002) is then stablished in the area, which stresses the role services play, mainly the ones that originate from university hospitals. This is the focus of the work developed by Djellal and Gallouj (2005) and by Windrum and García-Goñi (2008). They show that the hospitals that are home to high complexity treatments and/or research in the health sector often interact with the pharmaceutical, the medical and the medical equipment industries. Furthermore, the increasing incorporation of microelectronic devices to machinery and equipment contributed not only to the wide range of possibilities that unfolds in telemedicine, but also to the growing interaction between the medical sector and information and communication technologies.

Given the complex interaction between industry and services, one faces a typical evolutionary situation, in which learning mechanisms, especially the ones in clinical testing phases, involve a set of necessary adaptations in order to achieve success (Nelson *et al.*, 2011). In other words, there are important "learning-by-doing" and "learning-by-using" mechanisms that support incremental innovations until inventions that are often developed in university laboratories are transformed into new products and processes in the medical field.

The distinctive features of innovation in the health sector, in particular the content of interactions and the importance of institutions are highlighted by Consoli and Mina (2009). For these authors, innovation systems in the health sector are driven by a combination of interactions between agents shaped by institutions (innovation "gateways") and change patterns that feature a strong path dependent character (innovation "pathways"). There is, therefore, a complex structure of feedbacks that occur through interactions and knowledge transfer between research and clinical practice.

Metcalfe, James and Mina summarise the arguments above:

> [...] innovation in medicine is a process that is distributed across time, space and epistemic and institutional domains; that it entails the entrepreneurial effort of creative individuals as well as the emergence of correlated understanding among heterogeneous agents whose rules of interaction are contingently instituted in socio-economic systems along unfolding scientific and technological trajectories (2005, p. 1283).

By bringing together a set of contributions to innovation in health services, Thune and Mina (2016) reinforce the notion of hospitals as central actors. For these authors, these institutions assume several functions in the health innovation system: large health service providers; users of new technologies, generating an external demand for innovation; and potential developers of organisational innovation processes. In addition, the hospitals, as part of the educational system, constitute a training space for new professionals; they may also be *loci* of clinical trial and major R&D institutions. Therefore, for the authors, hospitals in general, but particularly teaching hospitals, become the central nodules in health networks insofar as they perform these many roles, and play thereby a key role in health innovation systems. Especially, university hospitals act as intermediaries between different domains and sources of knowledge, such as the scientific, clinical, technical and commercial. They are also bridges between different learning methods (through medical practice, basic and applied research). They also link the health systems in different phases of the innovation process, as they may be involved in the generation of ideas, in verification or tests stage, in implementation, and in dissemination.

Given the central role of hospitals, especially the university ones, as environments of generation and selection of innovations, and following the arguments by Thune and Mina (2016), further research becomes necessary.

Added to this argument, as justification for the present paper, is the fact that the various types of interactions and knowledge generation that bear innovation in the human health area are generally not present in developing countries. There is a set of historical-structural aspects that prevent/limit the development of health innovation systems that are appropriate for their demand structures. Although of the utmost importance in order to promote innovation systems in health sector that have as reference the specificities of developing countries, studies dedicated to this theme for the Brazilian case are still scarce and quite recent.

Chaves and Albuquerque (2006), by discussing relations between scientific and technological activities for the health field in Brazil, show that there is a disconnection between these activities. If, on the one hand, there is low scientific production, insufficient to trigger a virtuous circle that generates technological production; on the other hand, the local technological production is equally small and insufficient to stimulate the creation of new scientific research fields.

Part of the studies adopts the notion of the Economic-Industrial Health Complex (CEIS), aiming to investigate the interactions between the industrial base that produces goods (of chemical and biotechnological base and of mechanical, electronic and materials base) and the service provider sectors (hospitals, clinics, diagnosis and treatment services), which are consumers of manufactured goods from the first group and, at the same time, articulate the citizens' consumption of these industrial products (Gadelha, 2003; Barbosa; Gadelha, 2012).

According to Albuquerque and Cassiolato (2002), CEIS industrial subsystems in Brazil present features like: i) a chemical-based industry, producer of pharmacological products, mainly made up of multinational companies, whose research and development activities (R&D) focus on their countries of origin; ii) a small mechanical, industrial, electronic, and materials-based industry, in which much of the demand is met by imports. These characteristics significantly limit the interactions that could generate innovative dynamic to the health innovation system.

Paranhos and Hasenclever (2011) detail these aspects by showing that national pharmaceutical companies interact in a very limited way with universities, which differentiates them from companies from other countries. The focus of these companies on the production of generic drugs - which do not represent innovation for the market -, its small size and financing difficulties are the main explanatory factors for a low and little complex interaction pattern and the low volume of R & D spending.

Vidotti *at al.* (2008) reinforce the Paranhos and Hasenclever (2011) conclusions on the low innovative content of the Brazilian pharmaceutical industry. When analyzing the relationship between the new drugs launched in Brazil between 2000 and 2004 and the diseases that most affect the population, the authors concluded that most of them were not new in therapeutic terms.

When considering the differences in health innovation systems between developed and developing countries, Hanlin and Andersen (2016) defend the argument that innovation in the medical field should contemplate what they call "social innovation". Using examples of improvements to health systems in countries such as Cuba, Bangladesh and India, focused on a set of organisational and institutional innovations, the authors show that medical innovation must go beyond the offer of new technological developments in products. Thus, the strengthening of health innovation systems through the expansion of service coverage and increase of resources intended for the area require, according to the authors, not just technological solutions, but also institutional and organisational innovations.

Strengthening innovation systems in medium and low income countries supposes, according to Hanlin and Andersen (2016), focus on four elements called the "4 Fs": i) Function: inclusive development, with the objective of putting a broader perspective upon sectorial issues and focus on equity; ii) Form: recognition of the multiple actors involved in social and technological innovations; iii) Field: recognition of the market and other institutions ability to determine the field where the activities happen; and, iv) Flows: the most important among them, it relates to means in which there is knowledge exchange, through the connections and the flows that are originated and can be strengthened within the system, in order to articulate the actors (fields) and institutions (forms) for the improvement of health and welfare systems (function).

In this regard, a recent report by Unctad (2011) brings a set of evidences about the evolution of the pharmaceutical industry in five developing countries, namely Argentina, Bangladesh, Colombia, Ethiopia and Indonesia. In these countries, the local pharmaceutical industry has been able to have important market shares and, more importantly, to meet local health needs. These results are related to strategies to expand local capacities and to adapt the transfer of foreign technology to local needs, bringing policy coherence between industrial policy and public health.

The necessity to change the form that health innovation systems are analysed is also object of research in Cassiolato and Soares (2015). The authors criticise the conventional approach, in which the focus of actions is the disease and not the well-being in a broad sense. According to the authors, such approach focuses strongly on the development of new and improved technological solutions, which transforms big companies, especially those in the pharmaceutical sector, into the system's centre. On the other hand, promoting a well-being system, in which decreasing inequalities in access is the central element, demands not only technological solutions, but also organisational changes and emphasis on qualifying the agents.

3. Methodological Procedures

This study derives from the analysis of data collected from the DGP/CNPq. The selection of the research groups to be investigated was performed based on this information and on the results that Tatsch, Ruffoni and Botelho (2016) presented[3]. The procedures are explained below.

- Data from DGP censuses — the ones from 2010 and 2016 — were taken into account. The chosen groups were the ones that had interactions with organisations in a broad sense, in both periods, which increases the possibilities of selecting groups with a continuous practice of interaction, including at the present time.
- A further criterion of selection was the presence of the actor "hospital" among the interactions of the research groups.
- 20 groups were identified altogether, though two of them were inactive. Therefore, 18 group leaders were emailed and invited to participate in the study.
- The number of groups that were invited to participate in the research was expanded due to a suggestion from one of the respondents. In this case, the *snowball* was used. These are the cases of groups D and E. Although these groups had not been identified in the networks handled by Tatsch, Ruffoni and Botelho (2016), they were mentioned during an interview with another leader. Thus, given the relevance of these groups' performance, with regard to the intellectual production of their members, as well as to the interactions they establish with hospitals, it was decided to include them in the sample.
- Considering the response obtained from contacting the research group leaders, it was possible to carry out interviews with 5 of them.
- The interviews took place in early 2017. In order to guide the interviews, which were recorded, a script containing questions based on the theoretical framework was elaborated. Once the interviews, which had the duration of 1 to 3 hours, were carried out, they were transcribed and analysed.

Throughout this text, the five groups are indicated by the letters A, B, C, D and E, in order to protect their anonymity. On the basis of the information registered in the DGP/CNPq, it was able to make a general characterisation of the groups under analysis, which is presented below.

Group A was formed in 2003 and works in medicine. Since its foundation, the group has had professors qualified at all levels in the medicine field in its leading position. The group's research fields are composed of molecular biology of the attention deficit hyperactivity disorder (ADHD); clinical phenomenology of ADHD; therapeutic interventions in ADHD and neurobiology of ADHD. In 2004, its first year of participation in the *Census* of the DGP, the group had 30 participants, of which 5 were researchers, 16 students and 9 technicians. In 2016, the number of participants reached 68 members, being 25 researchers, 42 students and 1 technician. The group has a previous history of interaction with private companies, especially those active in the pharmaceutical area, all of them including financial remuneration and involving relationships of technical advice and scientific research, whereas there is no intention of immediate application of the results. The bibliographical production of the group is considerably expressive. It holds intellectual property rights of software created in partnership with private companies.

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[3]It is important to regard the conclusions that Silva Neto *et al.* (2012) drew in their research. As these authors proved, DGP underestimates the interactions in the field of health knowledge. They clarify that the type of connection that exists between universities, research institutes, hospitals, clinics and medical centres is not being properly captured, since research groups' leaders might not consider these institutions as companies. Still, DGP is the only official database available with historical series that report on characteristics of research groups in Brazil.

Group B was founded in 2005 and works predominantly in the field of collective health. It is led by two professors, one qualified in physical education[4] and another qualified in the field of electrical and materials engineering. Its lines of research include hospital biomechanics; development and application of neuromodulation techniques in rehabilitation; assistive technology for the treatment of critical adults; assistive technology for the treatment of urinary incontinence in women and assistive technology for the treatment of osteoarthritis. In 2016, the group was composed of 24 participants, of which 13 were students and 11 were researchers. The group's interactions, all classified as scientific research relationships, are performed with institutions of higher education and hospitals and they do not include resource transfers of any kind. This group owns nine registered patents.

It is important to point out that the interviewed leader chose to explain more about the research being currently developed by Group B and less about research conducted by the previously identified group. According to him, this group, whose object of investigation is assisted technologies, is more active at present. However, while giving his report, he also mentioned events and experiences that arouse from the first identified group, and these were also included in this text.

Research group C was formed in 2007 under the leadership of a professor educated in all levels of the medicine field. He is also a professor at the Federal University of Rio Grande do Sul (UFRGS), where he holds a chair in medicine. The other group leader, also educated in medicine, is not a professor, but a physician hired by Hospital de Clínicas de Porto Alegre (HCPA), a major university hospital in the capital of the state. During his period of practice, the group kept interactions with a university hospital in the areas of scientific research and personnel training. His lines of research are bariatric surgery - obesity; metabolic surgery; laparoscopic surgery; abdominal wall defects and surgical oncology. In 2008, the group consisted of 5 participants, i.e. 2 researchers and 3 students. In 2015, the group had 3 researchers and 3 students. The interactions of this group were classified as follows: scientific research without intention of immediate application of the results, scientific research results with intention of immediate application of the results, personnel training of the partner by the group, including in-service courses and training.

Unlike the groups mentioned above, group D does not fit in the field of health sciences, but in the field of biological sciences/pharmacology. It was formed in 2006 under the leadership of a professor detaining a undergraduate degree in biology and a graduate degree in biochemistry, with focus on neurosciences. Between 2006 and 2010, the group conducted research on preclinical pharmacology of bombesin/GRP receivers; preclinical pharmacology of glutamatergic receptors; molecular mechanisms of synaptic plasticity and memory; molecular mechanisms of the effect of anticancer drugs; animal models of psychiatric and neurological disorders and neuro-oncology. In this same period, the only interaction reported was one with a company active in the sector of scientific research and development. Currently, it conducts research on the biology and pharmacology of embryonic neural tumours; molecular biology of memory; genomics of receptors of the immune system; and signage by neurotrophin and neuropeptides in cancer. In 2016, the group consisted of 8 researchers and 13 students, amounting to 21 employees. At present, it comprises around 30 participants. Still in 2016, the interactions performed were exclusively with hospitals in scientific research and involved the transfer of financial resources and material supplies

[4] This researcher is also the leader of another group, which was initially identified through the work of Tatsch, Ruffoni and Botelho (2016). This group, whose lines of research include neuromechanics of human movement, neuromuscular plasticity and the trauma-orthopaedic rehabilitation, was founded in 2000. It belongs to the field of health sciences/physical education. Its interactions occurred not only with private companies, but also with a hospital and a higher education institution. These partnerships included scientific research, staff training and non-routine engineering activities, all without the transfer of resources, involving exclusively risk relationship. In terms of human resources, the group performed a considerable growth: it counted with 11 employees in 2000 and with 47 in 2016.

and provision of grants. In addition to the significant intellectual production, the group owns four registered patents.

Group E was founded in 1997 under the leadership of a professor with undergraduate and masters titles in medicine. It carries out research on the line of pathophysiology and bipolar disorder clinic. In 2006, first year of participation in the *Census* of the DGP, the group had 19 participants: 16 researchers and 3 students. Since 2010, the group is led also by a professor graduated in medicine with a doctorate in biochemistry. In 2016, there were 23 participants, of which 11 were researchers and 12 students.

4. Results Discussion

Multidisciplinarity is a feature of most of the investigated groups (A, B, D and E); only C is composed of researchers that are physicians only. In group A's case, also professors for psychiatry, genetics, and professors that work in the department of biology and molecular genetics and in the education faculty participate in the research. Physical educators, physical therapists and engineers are involved in group B. Group D counts with the participation of biologists, physicians, biomedical physicians, pharmacists, and biotechnologists. Physicians, pharmacists, biomedical physicians, a physiotherapist, a physical educator, a journalist and professionals with a language degree collaborate with group E.

Regarding **interactions/partnerships with hospitals**, it was observed that these are the most highlighted by the consulted groups. This type of partnership occurs especially with HCPA, UFRGS's teaching hospital, which is the university where lecturers/researchers, group leaders, are linked to. It is possible to consider, therefore, the establishment of such partnership as a truism. However, it must be mentioned that there are many other professors/researchers in the human health area, also research group leaders in UFRGS, which have no such insertion in the hospital.

It is important to reinforce that all five leaders that were interviewed have given special emphasis to their interaction with HCPA. One of the leaders even said that his group would not exist without the hospital.

HCPA was founded in 1970 as a public company under private law. It has its own net worth and administrative autonomy. It promotes practical teaching activities in partnership with UFRGS's courses: medicine, nursing, biomedicine, biology, physical education, pharmacy, nutrition, dentistry, pedagogy, and psychology. It offers around 50 medical residency programs, in 25 fields.

HCPA has an Experimental Research Centre that offers infrastructure with six multi-user laboratories and 20 themed laboratories. This centre aims to conduct basic and applied experimental research and to develop and enhance human resources for experimental research. There is also the Clinical Research Centre, whose objective is to promote the development and qualification of clinical trials at the hospital. It provides infrastructure to perform all stages on epidemiological and clinical studies. Both centres support emerging and consolidated research groups by providing adequate physical space.

With installed capacity of about 900 beds (with the ones from Intensive Care Unit), being more than 85% intended for patients of the Brazil's public health system (SUS), the HCPA is a highly complex national reference hospital. In addition to the beds, the structure of HCPA also has 40 operating rooms, 146 rooms to ambulatory attendance and 13 emergency rooms. At the time, new buildings are being built; which will increase the current area by almost 70%. It has more than 6000 employees.

It is also highlighted that HCPA is reference in management and plays a relevant role in the Ministry of Education's National Recovery of University Hospitals Programme (REHUF). It was chosen by the federal government to transfer its management model to other university hospitals from the network. Such excellence was certified in 2013 by the Joint Commission International, one of the groups providing international healthcare accreditation services to hospitals worldwide. Such seal of approval is a pioneer achievement among Brazilian university hospitals.

According to group A, C, D and E's respondents, the hospital's almost full-time operation is interesting, among other reasons, due to the specificities of HCPA's institutionality, which has administrative financial autonomy regarding the university. It makes the cases' processing faster, facilitates the establishment of covenants and fundraising. Two leaders of the health sciences/medicine groups, plus the one of biological sciences/pharmacology, have even their working offices in the hospital. Group E's leader adds that HCPA is very efficiently managed, which assists researchers to focus on research, not having to worry much with bureaucracies.

Group A operates in HCPA through a laboratory of ADHD patients' assessment from SUS. It also interacts with other teaching hospitals from other universities, such as the University of São Paulo (USP), the Federal University of Rio de Janeiro (UFRJ), and the Federal University of Pelotas (UFPel).

The interaction between group B and HCPA initially occurred with the hospital's biomedical engineering area, due to technical support provided by a hospital's engineer to equipment maintenance of the research group. According to the leader, professionals of HCPA's biomedical engineering area were trained, because "they had the knowledge to open an imported equipment, see what the problem was and identify solutions". It reflected, thus, their capability to perform reverse engineering. According to the respondent, there is important equipment construction expertise in this hospital's sector. In the research's current phase, hospital's biomedical engineers still play a key role, via prototypes construction, though which the interaction with HCPA expanded. Now it also aims an interaction with users. This must be done through the participation of Intensive Care Unit (ICU) patients on equipment testing. First, HCPA's ICU patients will participate in the study; and, further on, ICU patients from other teaching hospitals – Santa Casa Complex, Cardiology Institute and São Lucas Hospital – will also be incorporated to the testing.

In HCPA, group C researchers and physicians work in abdominal surgery service, attending to patients from SUS. Such service performs outpatient diagnosis and test analysis and, above all, treats these patients with highly complex surgical procedures. They perform bariatric surgeries and surgeries for abdominal wall defects. In addition to working in this service, the group's researchers also participate in the laboratory of experimental research in HCPA's surgery field (infrastructure shared by teams of surgeons from various specialties).

Meanwhile, group D coordinates a thematic experimental laboratory (related to cancerous tumours and Neurobiology) at HCPA. The leader explains that the group has strong support from the Children's Cancer Institute, a private non-profit entity, located within HCPA, which has been operating for 25 years. The institute is supported entirely by donations from the private community, companies or people, with or without tax exemption. According to the respondent, the service offered by the institute is excellent. They cure up to 70% of the children attended there (this average in RS revolves around 40%). As of a certain period, the institute made the decision to invest in biological research and started to support the group that focused on children's cancer research, more specifically children's cancer biology, aiming to discover new treatment alternatives.

Group E assesses patients from SUS via ambulatory, coordinates experimental themed laboratory focused on research on bipolarity (where the counter studies take place), and conducts clinical trials at the hospital's Clinical Research Centre.

The leaders reinforced yet the importance of HCPA as a learning and qualification space. According to all the respondents, HCPA has a relevant role in Rio Grande do Sul's educational system, in the health sciences field. There, undergraduates, graduate students and residents in several specialties are qualified. Health professionals from different areas are also trained.

Still regarding the ***interaction with patients***, as reported, such interaction occurs with patients assessed in HCPA's own ambulatories, via SUS, but also via epidemiological and clinical trials conducted at this hospital, but not only. The group, for example, through partnership with researchers from the UFPel, conducts epidemiological research (cohort studies) on the population of this municipality in Rio Grande do Sul's countryside. Still concerning cohort studies, this group counts with international partnerships with the aim of collecting data from patients of other locations. Group C, on the other hand, accesses data from patients treated there through researchers that are partners of the Federal University of Rio Grande (FURG), via their respective teaching hospital.

As for ***interaction with other researchers***, the groups identified it as very important for the construction of the generated knowledge. The partnership relation with other researchers and groups is granted special mention by the leaders. It was highlighted how relevant the information and knowledge exchange between reference groups is, not only in Brazil, but also abroad. To seek interaction with international institutions and researchers who work at the border is, without a doubt, according to the leaders, an opportunity to make progress in investigations and in generation of scientific knowledge. The cognitive proximity is an important element that explains the existence of this kind of collaboration.

The importance of these partnerships was emphasized by the leaders of groups D and E as they commented on the creation of the National Institute of Science and Technology in Translational Medicine (INCT-TM), which brings together researchers from several Brazilian universities that cooperate with one another and with further national and international researchers. The INCT-TM was created in 2009. Its participating institutions are: UFRGS (initial headquarters), the Federal University of Rio de Janeiro (UFRJ), the University of São Paulo-Ribeirão Preto (USP-Ribeirão/current headquarters), the Pontifical Catholic University of Rio Grande do Sul (PUCRS), and the University of Southern Santa Catarina (UNESC).

In relation to ***interactions/partnerships with the manufacturing industry,*** be it with pharmaceutical, medical equipment, or other segments, it was observed that, although these relations happen, they are less frequent.

Among the five investigated groups, the interaction with the manufacturing industry occurs regularly only in group A. In this case, partnerships with private companies, especially with the pharmaceutical industry, usually occur when these have some interest in aspects of ADHD treatment, whether they include medicaments or not. All of them are multinationals operating in Brazil, whose capital originates in countries such as Belgium, Switzerland, England, and the USA. In order to establish the partnership, the initiative must always come from the research group. The partnerships are stable and have been occurring with four pharmaceutical companies for a considerable amount of time. The interaction usually takes place with their departments of neurosciences.

According to the respondent, the interaction with these firms is not of the kind in which the industry hires their service to conduct a clinical trial, i.e. a trial that seeks a medication's approval by regulatory authorities, such as the National Sanitary Surveillance Agency (Anvisa), in Brazil, and the Food and Drug Administration (FDA), in the United States. In the leader's words, the group does not work with private sector demands, i.e. as a "service provider" to the industry. Such demands usually seek partnerships in order to carry out studies that will evaluate a new molecule with attention deficit, so that new drugs are approved by regulatory authorities. In those cases, the firms seek a significant number of patients around the world for testing and provide funding, so that the research group includes patients and gathers data. Both the research hypothesis and the protocol, though, belong to the firm. On the other hand, the leader explains that the group works with a different "design" for each of its partnerships: an "independent investigation protocol", where the hypotheses are managed by the research group. In other words, the hypothesis may involve a part of the company, but it is formulated by the group; the project is designed

by the researchers and the results belong to the group. Yet, according to the leader, the firms support such format, because the results may be interesting for them as well. In his words: "our idea is to generate hypotheses to be scientifically tested and seek partnerships that are necessary to achieve it".

For example, the leader commented the following situation: the group constructs a hypothesis about the responsibility of a particular gene in regulating the response to the medication. As a result, a protocol is elaborated by setting the number of patients who will receive medication during the study, seeking to evaluate this gene's *performance*. That is when the companies come in, which can either donate the medicine during the research or provide funds for its purchase.

In most cases, the support comes as funding for the group. Funding in two ways: either via support for research or as educational budget. In the latter case, they are not educational events with target audiences defined by the industry, but with an "*unrestricted grant*" scope, i.e., the budget is provided by private companies without their participation in determining the educational content. The leader cited, as an example, a project to promote education on attention-deficit and hyperactivity disorder in public schools, in partnership with the state department of education. The budget provided per company enabled the project. Another example would be the qualification of teachers, from a program proposed by the group and not by the industry. In this case, the companies' interest is to increase the market awareness of the disorder.

In the case of research projects in partnership with the industry, the interest of companies is to associate their image to a group that is internationally recognised as a knowledge generator in the ADHD research field. To illustrate, the leader mentioned a project that examined the prevalence of attention deficit in motorcycle couriers. The hypothesis would be that motorcycle couriers, given the way they drive, feature ADHD clinical condition, since they present signs, in general, of impulsivity and cause a significant amount of traffic collision. In this project, there was also a partnership with a company in the automotive industry, which provided for motorcycle riding simulators. We used two groups for testing, one receiving medication and another placebo, in order to assess whether the medication improves the rider's performance or not. In the respondent's view, the partner company, which provides the medicine, envisions a space in the market to be conquered. According to the leader, the project's result may originate a governmental program for medication use, which, consequently, affects the demand for drugs.

Group E also reported interaction with multinational companies, producers of pharmacological products, both for clinical trials initiated by researchers and those proposed by the industry. In the latter case, the interaction occurs through a clinical trial that follows predefined protocols. In these studies, the company defines the protocol that determines which individuals can participate in the trial, which medicines and dosages will be used, and also the time of duration of the study. For the leader of this group, this situation, in which the group is a service provider, configures itself as an opportunity to obtain applicable resources in items that traditional agencies do not fund, such as maintaining an efficient administrative team to support the management of the group.

Concerning group A, the researchers developed an app in partnership with private companies from different segments: multinational pharmaceutical subsidiary in Brazil, specialized in biopharmaceuticals (that funded the project); information technologies service company from São Paulo, the software developer; national time management consultancy company; and British multinational, which assists in content providing. The app, which can be downloaded for free, has several features: it offers information on ADHD, treatment monitoring, symptoms assessment, among others. The app registers the patient’s information as a type of record by creating a dashboard — an indicators panel with consolidated information and made available in an easy-monitoring screen —, assisting the physician in the patients' treatment. The group understands that the use of the app by the patients will allow a Big Data collection, which will be very useful for future research. The app's copyright (intellectual property) was registered.

While groups C and D leaders reported not interacting with private companies in this industry, group C leader commented that, although they could seek partnerships of this kind, they have difficulty devoting time to prospect for potential partners. Added to that, according to him, is the fact that partnerships of this nature are badly seen by the scientific medical community. In his words, "there is prejudice", since most of the times Big Pharma imposes conditions that take the researchers' freedom. Anyway, in the past, they had a successful partnership experience with a manufacturer company of material for obesity treatment surgeries. This national capital company sought to validate the effectiveness of a product (an intragastric balloon) by Anvisa and, therefore, it needs to be tested. There was, then, the collaboration of the group at this stage, by performing tests in patients operated in the HCPA and also in a private hospital. From then on, the product came to be adopted routinely in surgery. After this experience, group C set no more interaction with industrial companies.

Group D's leader reported they never interacted with pharmaceutical laboratories. He clarifies that, given the characteristics of the research they develop, there is still a long way to provide results that can be applied by the industry. According to him, they are still in a stage of basic research ("counter studies"), "of discovery, seeking to develop better strategies of experimental new drugs". On a brighter note, he commented that the group has already originated two start-ups, considered spin-offs. Both were incubated at UFRGS. One of them has already been closed and the second is currently incubated at the University of São Paulo (USP). The latter has at least three patents deposits and is in prototype testing phase.

Group B's leader, on the other hand, commented that in the past he has contacted national private companies in order to produce already tested prototypes in scale. However, negotiations were not successful. According to him, usually there is not a convergence between the interests of private firms and universities/research groups. Besides, he believes that national companies have little capital to invest in R&D and certain aversion to risk.

Finally, concerning ***funding***, it is important to highlight that, in all of the respondents' views, the federal agencies that encourage scientific and technological research, such as CNPq and CAPES[5], as well as state agencies such as Foundation for Research Support of the State of Rio Grande do Sul (FAPERGS) and Foundation for Research Support of the State of (FAPESP) are important funding organs. All leading researchers avail of productivity grants from CNPq, as well as participate in grant programs.

They stress, however, that the bureaucracy to plead resources and accountability, as well as the casting of headings and difficulties to import equipment and materials, impose bottlenecks and constraints that hinder the smooth running of research.

Group A's leader commented that, in order to escape the casting of funding agencies, they seek to take advantage of partnerships with companies to gain access to resources that are more flexible and that allow greater flexibility in their use. He classified such resources as "soft Money". According to him, the amount is not so expressive, but enables trips, participation in events, and other activities considered relevant to the scientific knowledge construction and transfer.

Group E's leader, in turn, added that they adopt the strategy of seeking resources in international agencies, so they can have access to more significant funding and flexibility in their job. She commented that such resources, for example, help in hiring participants of the team; which facilitates the creation of a long-lasting staff.

[5] Government agency linked to the Brazilian Ministry of Education in charge of promoting high standards for post-graduate courses in Brazil.

In group D's case, their research's funding comes from both these resources from public agencies, from HCPA's own research fund, and from donations performed by the community to the Children's Cancer Institute and channelled to the experimental laboratory.

This fund, owned by HCPA itself, finances research projects from the hospital's employees. The selection is performed based on a series of criteria, which favour meritocracy. The leaders also commented on the hospital's efficiency in managing resources, whether they come from the fund or from external bodies and are managed on the medical foundation of HCPA.

Considering what was exposed, ***reflections*** are presented below to answer the proposed research problem: *Which features are presented in the interactions between universities and other organisations with regard to knowledge generation and innovation in medical assistance, products and/or processes in the health sector?*

As the literature points out, the varied formations characteristic of the research groups' teams was verified as important requirement to the process of scientific and technological development in the area. Both the participation of different institutional actors and the multidisciplinarity in the teams' formation were observed, since the research groups involve participants from different areas of knowledge.

As for the wide range of organisations involved, the literature that analyses the health field from the innovative systems approach gives special emphasis to the role of hospitals and, in particular, to university hospitals. Accordingly, Thune and Mina (2016) indicate that hospitals with a strong focus on learning have more relevant innovative *performances*. This point is reinforced in the results of this research, since a relevant role of interaction and research space for knowledge and innovation generation was assigned to HCPA, UFRGS's teaching hospital. As a result, the hospital benefits from the research's results and findings, via an improvement of its services.

The importance of HCPA, as *locus* of research and experimentation, is due to two reasons. First, the experimental and clinical research laboratories, where the groups work, are located in HCPA itself. Secondly, the hospital ensures the opportunity for researchers to be in contact with professionals from different areas, as well as with patients. This reality applies to the five investigated groups; majorly to groups A, C, D and E's cases, but also to B's, which, even though their laboratory is not located within HCPA, avails of HCPA's patients to test their equipment.

From the analysis of group C's *modus operandi*, it is possible to verify, on the one hand, the importance of the interaction with patients for the research group's knowledge generation, and, on the other, the importance of the role played by the hospital in the context of the users, result of the development of a range of innovations in services for the support of new treatments. Group C has shown that the experimental practice may lead to generation of new ideas, both in terms of existing services and techniques and completely new ones. Also group D, when it comes to their more clinic-oriented studies, has created new procedures for treating children patients with cancer. Group E also stressed the importance of contact with patients through service via ambulatory as well as through clinical research, for knowledge generation that result in advances in treatment. Such findings reinforce ideas present in the literature; as, for example, the ones in Thune and Mina (2016), who emphasise that hospitals are sources of new ideas and channels to innovations generated elsewhere in the health innovation system. Therefore, their contributions' analysis must be understood in relational and co-evolutionary terms. Also Consoli and Mina (2009) emphasise that hospitals are the location of clinical practice, being the largest channel for the revelation of new treatments' potential, as well as for the disclosure of its disadvantages, and are the location where observations are made to assist in the formulation of new ideas for treatments.

Another identified characteristic was the relevance of interaction with patients for all groups. This

importance is related either to the fact that patients participate in the research's testing stages, provide biological inputs for the research development, or that their service allows research hypotheses to be built. It was found, in summary, that the feedback of interaction with these users affects the direction of research and innovation efforts. Often, such access to patients occurs via HCPA itself, but not only. Again, this result is consistent with the findings of other authors, as Gelijns and Rosenberg (1994), who describe innovation in health sciences as a dynamic process influenced by the interaction between developers and users. There are also other works by Consoli and Mine (2008), Nelson *et al*. (2011), and Thune and Mina (2016) that present similar arguments on the role of patients as participants in the medical innovation process.

As in Nelson *et al*. (2011), that indicates the existence of multipath ways and mechanisms involved in the evolution of the medical knowledge and in the medical practice, this research also identified the characteristic of varied paths in the operation dynamics of the analysed groups. These authors suggest three paths to medical progress: scientific advances, responsible for greater understanding of the human body and the diseases pathologies; the advances in the technological capabilities, which allow the development of new methods of treatment and medical diagnosis; and the learn-by-doing method, via clinical practice learning, allowing advances in diagnoses and treatments. They add that these are interdependent paths in the speed and direction modelling of the medical practice innovations.

Another feature that emerged from the research was the scarcity of partnerships with the industry, as pointed out by Paranhos and Hasenclever (2011). Such a situation was normally assigned either to the characteristics/phase in which the research is (when considered basic and still in a much earlier stage to a possible interaction with Big Pharma; there being, therefore, results consolidation stages still ahead); or the difficulty of reconciling the interests of groups and companies. The university's bureaucracy was also cited as a deterrent; as well as the lack of funding capacity of the national industry. Added to that, the fact that R&D labs of multinationals are generally located next to their headquarters must be taken into consideration, since this imposes a geographical distance and also raises difficulties for cultural interaction. As Crescenzi, Filippetti and Iammarino (2017) point out, U–I collaborations are less likely to happen when compared to collaborations involving exclusively university partners of business partners, for exemple. Thus, the lack of collaboration university-industry can be also related with absence of institutional proximity.

Such disconnection among those who generate knowledge in the universities and industry is pointed out by the literature that analyses the reality of developing countries. To this end, Chaves and Albuquerque (2006) conclude that there is a disconnection between the scientific and technological production in the health sector's innovation system of the country. The research confirms that conclusion since the analysed groups have high scientific production and very low interaction with industry, conforming an immature innovative system, typical of emerging countries (Albuquerque, 1996; 2009).

In other words, we can say that differently from what occurs in developed countries, where the innovations in the medical field "[...] are increasingly dependent on the interaction between the clinical delivery of health care services and the manufacturing system that develops and delivers new drugs and new instrumentation and devices to enhance the delivery of clinical services [...] So close is the degree of supply chain interdependence that the medical service economy and the medical industry economy are effectively one" (Metcalfe; James; Mina, 2005, p.1301); in emerging countries, such as Brazil, this linkage does not fully occur yet.

Another important aspect related to the questions posed by Hanlin and Andersen (2016) and Cassiolato and Soares (2015), concerns a disconnection that occurs at the level of demands that are imposed on the health innovation system in Brazil and the performance of the research groups. As the case studies

analyzed by Unctad (2011) show, there are developing countries that have been able to improve their health innovation systems to meet local needs.

5. Final Considerations

As it was pointed out, according to the neoschumpeterian thought and to the innovative systems approach, innovations should be seen as a long-term problem-solving process, in which the collaboration between different participants and competences are key. In this sense, medical innovations are based on various sources of knowledge spread through a wide range of organisations — universities, companies, hospitals and research institutes — that are involved in their development and dissemination. Not only a considerable number of organisations is involved in this process, a variety of professionals from different areas is so as well.

Emerging (or "developing") countries have specific characteristics — pertaining culture and political institutions and policies —, that should be taken into account when analysing the particularities of their innovation systems and their ability of generating technological change.

The object of research in the present study was the interactions established by five health research groups within UFRGS. This university, as pointed out in another study previously mentioned, can be considered an interaction hub of the field in Rio Grande do Sul, since it concentrates the largest part of research groups and of other groups that interact in this field of knowledge in the state. This exploratory study identified important characteristics of the interactions established between the actors involved and seeks advances in medical care and in innovation development.

These characteristics are systematised below and corroborate at large other findings that have been already published in specialised literature:

- **Multidisciplinary researcher teams** qualify the process of generating knowledge and innovations;
- **The teaching hospital is the key actor**, be it as a (clinical or experimental) research space for innovation and knowledge generation, be it as a learning and training space;
- **Patients are relevant actors** in the establishment of interactions and generation of knowledge by the groups, whereas clinical research and assistance constitute important ways of creating new ideas;
- **Other researchers** from research centres or universities in Brazil and abroad participate in the process of knowledge generation. This situation points positively to the existence of a process of capacity building in the investigated scenario;
- **Industrial firms have little or no presence in the established interactions**, and important elements that may explain this situation are the research phase (basic level), the conflict of interests, the bureaucracy and the institutional frailties at different levels (that of the university, of the state and of the federation), the national industry's lack of funding resources and absorptive capacity as well as the geographical distance between R&D departments and their headquarters;
- **Disconnection between scientific and technological production**, since the investigated groups have high scientific production and very low interaction with the manufacturing industry. A chain of routines that target for the joint construction of knowledge and innovations with industry was not observed.

It is important to reiterate that the three paths mentioned by Nelson *et al.* (2011), i.e. scientific advances, advances in technological capabilities, and the learn-by-doing method, which shape the direction and speed of innovation in medical practice, were all clearly identified in the present study.

As to the specifics of the emerging countries, the results of this study relate, reiterate and complement the literature on the university-industry interactions in Brazil. Several studies point to the fact that these relations are still scarce in the scientific and technological scenario in the country. Over time, an institutionality, in the broad sense, that aims to promote fruitful approaches between these different actors in the innovation system, has to be built. That means to say, as Hanlin and Andersen (2016) put it, that it is necessary to enlarge the flows for knowledge exchange, in order to articulate the actors (fields) and institutions (forms) for the improvement of health and welfare systems (function). In order to achieve this, more than just technological solutions is necessary. New articulations between actors must emerge so that actions that focus on the reduction of global inequalities in health and welfare are created, as also discussed by Cassiolato and Soares (2015).

Another important conclusion, in terms of implications for public policies, concerns opportunities to make better use of the knowledge generated by the Brazilian scientific sector, which encourages the national industry to explore the opportunities created by research that was conducted by groups active in universities of our country. Besides that, it is necessary to promote political measures that encourage the creation of start-ups resulting from scientific discoveries in universities. This could foster new entrepreneurs and promote technological parks and spaces as incubators. This appears to be the path to be most emphatically pursued.

The international literature highlights, in particular, university-industry and service-industry interactions as keys to the scientific-technological progress in the health sector. On the other hand, this study's results showed that, in Brazil's case, such interactions are not frequent, while those between university-assistance play an important role for innovations in treatments. Advances on a theoretical framework that explores the peculiarities of emerging countries are therefore necessary.

Finally, it is important to mention that this study presents limitations, as any exploratory research that adopts the case-study method does, which makes it impossible for one to generalize their results. Pointing out this limitation intends to serve as a *stimulus* for the realisation of further investigative research of this nature, which may be conducted with other research groups from UFRGS or with groups linked to other universities and Brazilian regions.

6. References

ALBUQUERQUE, E. M. Sistema Nacional de Inovação no Brasil: uma análise introdutória a partir de dados disponíveis sobre a ciência e a tecnologia. **Revista de Economia Política,** vol. 16, n. 3, p. 56-72, 1996.

ALBUQUERQUE, E. M. Catching up no século XXI: construção combinada de sistemas de inovação e de bem-estar social. In: SICSÚ, J.; MIRANDA, P. (Org.). **Crescimento econômico: estratégias e instituições.** Rio de Janeiro: IPEA, 2009, p. 55-83.

ALBUQUERQUE, E. da M.; CASSIOLATO, J. E. As Especificidades do Sistema de Inovação do Setor Saúde. **Revista de Economia Política,** v. 22, n. 4 (88), outubro-dezembro 2002.

ASHEIM, B.; GERTLER, M. S. The geography of innovation: regional innovation systems. **The Oxford Handbook of Innovation,** Oxford University Press, Oxford, 2006.

BARBOSA, P. R; GADELHA, C. A. G. O papel dos hospitais na dinâmica de inovação em saúde. **Revista de Saúde Pública** 46 (Supl), p. 68-75, 2012.

CASSIOLATO, J. E.; SOARES, M. C. Health Systems, Development and Health - An introduction. In: CASSIOLATO, J. E.; SOARES, M. C. (Eds.). **Health systems, equity and development**. Río de Janeiro: E-papers, 2015, p. 15-57.

CHAVES, C. V.; ALBUQUERQUE, E. M. Desconexão no sistema de inovação do setor saúde: uma avaliação preliminar do caso brasileiro a partir de estatísticas de patentes e artigos. **Revista de Economia Aplicada,** v. 10, p. 523-539, 2006.

CHAVES, C. V.; MORO, S. Investigating the interaction and mutual dependence between science and technology. **Research Policy,** v. 36, p. 1204-1220, 2007.

CONSOLI, D.; MINA, A. An evolutionary perspective on health innovation systems. **Journal of Evolutionary Economics**, 19, p. 297–319, 2009.

COOKE, Philip. Introduction: origins of the concept. In: BRACZYK, Hans-Joachim; COOKE, Philip; HEIDENREICH, Martin (Ed.). **Regional Innovation Systems**. London: UCL Press, 1998. p 2-25.

COSTA, A. B. da; RUFFONI, J.; PUFFAL, D. Proximidade geográfica e interação universidade-empresa no Rio Grande do Sul. **Revista de Economia** / UFPR, v. 37, n. especial, p. 213-238, 2011.

CRESCENZI, R.; FILIPPETTI, A.; IAMMARINO, S. Academic inventors: collaboration and proximity with industry. **Journal Technology Transfer**, Volume 42, Issue 4, p. 730–762, 2017

DJELLAL, F.; GALLOUJ, F. Mapping innovation dynamics in hospitals. **Research Policy**, 34, p. 817-835, 2005.

DOSI, G. Technological Paradigms and Technological Trajectories: A suggestes interpretation of the determinants and directions of technical cahnge. **Research Policy**, 11, p. 147-162, 1982.

EDQUIST, C. Systems of Innovation: perspectives and challenges. In: FARBERGER, J.; MOWERY, D. C.; NELSON, R. (Orgs.). **The Oxford Handbook of Innovation**. Oxford: Oxford University Press, 2006.

FREEMAN, C. The 'National System of Innovation' in Historical Perspective. **Cambridge Journal of Economics**, 19, p. 5-24, 1995.

GADELHA, C. A. G. O complexo industrial da saúde e a necessidade de um enfoque dinâmico na economia da saúde. **Ciência & Saúde Coletiva,** v. 8, n. 2, p. 521-35, 2003.

GADELHA, C. (Coord.). **Perspectivas do investimento em saúde.** Rio de Janeiro: UFRJ, 2008 / 2009. Relatório final do estudo do sistema produtivo Saúde, integrante da pesquisa "Perspectivas do Investimento no Brasil", realizada por IE/UFRJ e IE/UNICAMP. Disponível em: http:// www.projetopib.org/?p=documentos

GADELHA, C. A. G. (Coord.). **A dinâmica do sistema produtivo da saúde:** inovação e complexo econômico-industrial. Rio de Janeiro: Editora FIOCRUZ, 2012.

GELIJNS, A.; ROSENBERG, N. The dynamics of technological change in medicine. **Health Affairs,** [s.l.], v. 13, n. 3, p.28-46, 1994.

GELIJNS, A. C.; ROSENBERG, N. The changing nature of medical technology development. In: ROSEMBERG, N.; GELIJNS, A. C.; DAWKINS, H. **Sources of medical technology: universities and industry.** Washington: National Academy Press, 1995.

HANLIN, R.; ANDERSEN, M. H. **Health Systems Strengthening. Rethinking the role of innovation**. Globelics Thematic Report 2016. Denmark: Aalborg University Press, 2016.

HICKS D.; KATZ, J. S. Hospitals: the hidden research system. **Science and Public Policy** 23(5), 297-304, 1996.

LUNDVALL, B-Å. Innovation as an interactive process: from user-producer interaction to the national system of innovation. In: DOSI, G. *et al*. (Eds.). **Technical change and economic theory**. Londres: Pinter, 1988, p. 349-369.

LUNDVALL, B-Å. (Ed.). **National innovation systems**: towards a theory of innovation andinteractive learning. London: Pinter, 1992.

MALERBA, F. Sectoral System of Innovation and Production. **Research Policy**, v.31, p.247–264, 2002.

METCALFE, J. S; JAMES, A.; MINA, A. Emergent innovation systems and the delivery of clinical services: The case of intra-ocular lenses. **Research Policy,** 34, p. 1283–1304, 2005.

MOWERY, D. C.; SAMPAT, B. N. Universities in National Innovation Systems. In: FAGERBERG, J.; MOWERY, D.C.; NELSON, R.R. (Orgs.). **The Oxford Handbook of innovation**. Oxford: Oxford University Press, 2006.

NELSON, R. (Ed.). **National Innovation Systems:** a comparative analysis. Nova York: Oxford University, 1993.

NELSON, R. R.; BUTERBAUGHB, K.; PERLB, M.; GELIJNS, A. How medical know-how progresses. **Research Policy**, n. 40, p. 1339–1344, 2011.

NELSON, R. R.; WINTER, S. G. **An Evolutionary Theory of Economic Change**. Cambridge, Mass./ London: The Belknap Press of Harvard University Press, 1982.

PARANHOS, J.; HASENCLEVER, L. The Relevance of Industry-University Relationship for the Brazilian Pharmaceutical System of Innovation. Pyka, A.; Fonseca, M. G. D (Eds) **Catching Up, Spillovers and Innovation Networks in a Schumpeterian Perspective.** Springer, 2011.

PAVITT, K. Sectorial patterns of technical change: towards a taxonomy and a theory. **Research Policy**, n. 13, North-Holland, 1984.

SILVA NETO, F. C. C. *et al.* Abordando os grupos de pesquisa sobre sua relação com as instituições: uma avaliação por area específica de conhecimento. In: **Anais…** XV Seminário sobre a Economia Mineira, Diamantina: CEDEPLAR / UFMG, 2012.

SUZIGAN, W.; ALBUQUERQUE, E. da M. The underestimated role of universities for the Brazilian system of innovation. **Brazilian Journal of Political Economy***,* v. 31, n. 1 (121), p. 3-30, January-March/2011.

TATSCH, A. L.; RUFFONI, J.; BOTELHO, M. R. A. Health Innovation System: networks in Rio Grande

do Sul/Brazil. **América Latina Hoy**, v. 73, p. 87-119, 2016.

THUNE, T.; MINA, A. Hospitals as innovators in the health-care system: A literature review and research agenda. **Research Policy,** [s.l.], v. 45, n. 8, p.1545-1557, out. 2016.

UNCTAD (2011). **Local Production of Pharmaceuticals and Related Technology Transfer in Developing Countries: A series of case studies by UNCTAD Secretariat.** United Nations, New York and Geneva, 2011.

VIDOTTI C. C. F.; CASTRO, L. L. C; CALIL, S. S.. New drugs in Brazil: Do they meet Brazilian public health needs? **Revista Panamericana de Salud Publica**, v. 24, p.36–45, 2008.

WINDRUM, P.; GARCÍA-GOÑI, M. A neo-schumpeterian model of health services innovation. **Research Policy***,* 37, p. 649–672, 2008.