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Construção e aprimoramento de capacidades por meio da aquisição de pequenas empresas: Um estudo da indústria farmacêutica

Construction and improvement of capabilities through the acquisition of small enterprises: an study about the pharmaceutical industry

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Resumo: Este trabalho parte da aquisição de pequenas empresas por grandes empresas como um fenômeno recente. A partir deste fato se pergunta: Que elementos são incorporados pela grande empresa que impactam positivamente sobre sua atividade inovativa? Dessa forma, o objetivo deste artigo consiste em responder esta pergunta. Para isso o estudo estabelece quais os elementos presentes na pequena empresa que podem contribuir com a atividade inovativa da grande empresa. Estes elementos são basicamente dois: uma contribuição de ordem técnica e outra de que incorpora as habilidades dos trabalhadores. A contribuição técnica advém dos resultados das atividades de pesquisa da pequena empresa, no presente caso, as patentes que são as técnicas em si e as capacidades para patentear, as quais estão descritas nas classes de patentes. A contribuição oriunda das habilidades pode ser observada através dos inventores que trabalham na empresa, como proxies para estas o estudo utiliza os inventores das patentes. Este estudo conclui que a contribuição técnica das pequenas empresas é utilizada para fortalecer as capacidades já existentes nas grandes empresas. Em contrapartida, a contribuição baseada em habilidades é utilizada de forma mais intensiva e para criar novas competências.

Palavras-Chave: Fusões e Aquisições, Pequenas Empresas Intensivas em Conhecimento, Patentes, Indústria Farmacêutica

Abstract: This study departs from the acquisition of small enterprises made by large enterprises. This phenomenon raises the following question: Which elements are incorporated by the large enterprise that enhance its innovative activity? Then the objective of this article is to answer this question. In order to do it, this study stablishes what are the mains elements present in the small firms that can enhance the large enterprise' innovative activity. These elements are a technical contribution and a skill contribution. The technical contribution is the direct result of small enterprises' search activities, in this case, patents. The skills contribution has its origins on the scientist that work for the small enterprises, in this case of this article, the patent inventors. As conclusion, this study states that technical contribution is mainly used to strengthen the already developed capabilities of the large enterprise. Nevertheless, the skills contribution is used more extensively and it can be used to create new competences.
Keywords: Mergers & Acquisitions, Knowledge Intensive Entrepreneurship, Patents, Pharmaceutical Industry.

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Introduction

Technological paradigms may suffer from diminishing returns as the technological trajectories within them are all explored. This process has been vastly discussed among the pharmaceutical industry under as the "famous" R&D productivity crises. (GAMBARDELLA, 1995; MUNOS, 2009; NIGHTINGALE, 2000; PAUL ET AL., 2010; SCHWARTZMAN, 1976, among others). The so-called productivity crises have not a unanimous cause, some authors stress the rising costs of developing new drugs (CARTER et al., 2016; COMANOR; SCHERER, 2013; DIMASI, 2000;GRABOWSKI and VERNON, 1994, 2000; MUNOS, 2009; PAUL et al., 2010), others addressed it as an exhaustion of the technological trajectories (ACHILLADELIS; ANTONAKIS, 2001; HOPKINS et al., 2013; NIGHTINGALE, 2000; among others). The only consensus is about how the industry is trying to overcome this problem.

The undergoing solution is through the diversification of its capabilities, mainly, the incorporation of biotechnologies in the drug discovery activities (DE MATOS, 2016; NIGHTINGALE, 2000; QUÉRÉ, 2004;GLEADLE *et al*., 2014; MALERBA; ORSENIGO, 2015).This process has begun when large enterprises built initial biotechnology competences internally. At first, the large pharmaceutical enterprises kept some research in biotechnologies inside and consequently some absorptive capabilities were developed allowing to keep up with the technical advance (COHEN; LEVINTHAL, 1990; SHARP, 1996). In a second moment, in the mid of the 1980s, the Big-Pharma started to interact with small biotech enterprises, in particular, through collaborations and acquisitions. Those interactions were attempts to internalize some critical biotechnology competencies (AHUJA; KATILA, 2001; CASSIMAN; VEUGELERS, 2007; CLOODT; HAGEDOORN; VAN KRANENBURG, 2006; HAGEDOORN; DUYSTERS, 2002a; MAKRI; LANE, 2007; MALERBA; ORSENIGO, 2015; POWELL et al., 2013; POWELL W.W. KOPUT, 1996; SHARP, 1996). In present days all Big-Pharma have some scouting team that looks for promising new technologies developed by small biotech companies.

Those scouting teams are institutionalized actions towards increasing the interaction with small biotech corporations (DE MATOS, 2016). Recently, the incorporations of new technologies, through acquisition of small enterprises, became a well-established behavior, up to 50% of the large pharmaceutical enterprises' new technologies were projects that started in small biotech enterprises (Matos, 2016).

The literature has not yet addresses this subject in a substantial way, some studies (AHUJA; KATILA, 2001; AHUJA; LAMPERT, 2001; CLOODT; HAGEDOORN; VAN KRANENBURG, 2006; GERPOTT, 1995; HAGEDOORN; DUYSTERS, 2002b) have dealt with Mergers and Acquisitions (M&A) driven by technological aspects, then ignoring the enterprise size. The few that are dedicates to small and large enterprises (such as: ANDERSSON; XIAO, 2016; BAUER et al., 2016; DESYLLAS; HUGHES, 2010; NORBÄCK; PERSSON, 2013; XIAO, 2014), unfortunately, are highly focused on post-acquisition performance measured through patents. This approach has two problems. First, the productivity problem is not a patenting activity problem, although this specific point is not the concern of this article. Finally, and the main concern of this article, post-acquisition performance is to consider the enterprises as black boxes, these studies are only seeing if the acquisition may or may not increase the patenting activity.

In order to overcome this black box problem this article poses some important guiding questions: what is incorporated by the large enterprises as they are acquire by small enterprises? And if small enterprises are acquired for increasing the large enterprises productivity, what are the elements in the small enterprises that can contribute the large enterprises innovative output?

The main objective of this article is answer these guiding questions. In order to accomplish the objective this article will set a sample of the most relevant large pharmaceutical enterprises. Through the sample, patent information about the large and small acquired enterprises will be gathered. The patent information will be analyzed according to two main concepts: technical contribution and skill contribution. Those concepts are fundamental for understanding what is held by the large enterprise when it acquire a small enterprise.

This article will be divided in three more sections and a conclusion. The first section will be dedicated to discuss the acquisitions driven by technological aspects and the inventor's role. This discussion will be the theoretical base for defining the main concepts. The second section will be the methodological remarks, where the sample will be defined, the process of data gathering will be presented and the way the data will be analyzed will be discussed. Section three will present and discuss the results and finally the conclusion.

1.1 The impact of M&A on the enterprises' innovative activities

The subject of M&A have long been addressed. Generally speaking, the enterprise that resort to M&A can grow by accumulating new resources from different and external sources and then expanding its knowledge base (PENROSE, 1959).The growing knowledge base can lead to new resources and then become new competences.

A vast literature is dedicated to understand what drives M&A. For instance, enterprises will merge or acquire others to access new markets, to increase their scales, to get a better financial position, to have access to technologies and many other motives. The important fact is that these drivers change according to sector, and enterprise size (CHAKRABARTI, 1995; GERPOTT, 1995). Arguably, the outcomes will, always, be the accumulation of new resources (PENROSE, 1959).

An especial kind of M&A are the ones driven by technological aspects, in which the new resources incorporated will increase the enterprise's innovativeness. (AHUJA; KATILA, 2001; ANDERSSON; XIAO, 2016; CLOODT; HAGEDOORN; VAN KRANENBURG, 2006; DESYLLAS; HUGHES, 2007, 2010; HAGEDOORN; DUYSTERS, 2002b; MAKRI *et al.*, 2010; XIAO, 2015). Among the M&A driven by technological aspects one can identify a especial group of acquisitions, the ones between small and large enterprises. The few studies dedicated on this subject are focused on empirical and sectoral studies (ANDERSSON; XIAO, 2016; CASSIMAN; VEUGELERS, 2007; DESYLLAS; HUGHES, 2007, 2010; EJERMO; XIAO, 2014; LAURSEN; SALTER, 2014; XIAO, 2014; among others) especially, because this kind of acquisition is, mainly, a high tech sector phenomenon. Therefore, this kind of acquisitions are prone to happen in a sector where small enterprises have a distinguished role in the technical progress.

In an post-acquisition analyses the incorporation of small enterprises have, indeed, shown a positive relation between acquisitions of small enterprises and an increase in the large enterprise technological output (AHUJA; KATILA, 2001; ANDERSSON; XIAO, 2016; DESYLLAS; HUGHES, 2007, 2010; HUSSINGER, 2010; SZÜCS, 2014). Arguably, the acquisition is a way of uniting different pieces of knowledge in one enterprise. By gathering those pieces of knowledge, the number of knowledge combinations are increased, thus, all these novel combinations can, possibly, leads to more innovations (AHUJA E KATILA, 2001; HAGEDOORN AND DUYSTERS, 2002; DESYLLAS AND HUGHES, 2008; MAKRI *et al.*, 2010). Therefore, the whole knowledge incorporated through acquisitions enable the company to create new products for the market and in some cases create new technological trajectories (HAGEDOORN *et al.*, 2002).

In order to analyze technological driven acquisition between large and small enterprises, one must consider the incorporation of capabilities of one company to another as a time consuming process without short-term effects over technology, which, in many cases, can disguise the real effect of acquisition (GERPOTT, 1995). Indeed, M&A driven by technological factors can only be analyzed through technological variables. Therefore, there is a necessity of using or developing measures based on knowledge features (De MATOS, 2016).

1.2 Knowledge base relatedness and the M&A success

Enterprises are entities that deal with knowledge (Nelson and Winter, 1982). For instance, when one enterprise acquire another, the acquired enterprise's knowledge can be accessed. The ability to access knowledge does not mean understanding and using it; for that matter, there must have some similarities between the two enterprises knowledge base. In essence, enterprises cannot deal with things that they completely do not know.

In order to use external knowledge for creating and enhancing capabilities, the acquiring enterprise must understand the general principles that rule the other enterprises knowledge base (AHUJA AND KATILA, 2001; DESYLLAS AND HUGHES, 2008; HAGEDOORN AND DUYSTERS, 2002; MAKRI *et al.*, 2010). Therefore, enterprises when engaging in horizontal and vertical acquisitions should enjoy some technological relatedness with their target (HAGEDOORN AND DUYSTERS, 2002).

Several studies attempt to create concepts and measures for the enterprises knowledge base relatedness. These concepts help understand how relatedness affect the enterprises' technological outputs. Nevertheless, all those ideas are based on the concept of absorptive capacity. In essence, the difference and relatedness between each knowledge base will lead to different degrees of assimilation (CLOODT AND HAGEDOORN, 2006; MAKRI *et al.*, 2010).

According to MAKRI *et al.* (2010); CLOODT AND HAGEDOORN (2006); HAGEDOORN AND DUYSTER (2002); AHUJA E KATILA, (2001) the difference in the technological and scientific knowledge between companies is an important factor in the process of technical change. The merger of extremely similar a companies would only generate duplication. Therefore, a difference between the enterprises knowledge is necessary to provide opportunities for learning, building and developing absorptive capacities (MAKRI *et al*., 2010). On the other hand, when companies are extremely different from each other, regarding technical knowledge, the process of M&A becomes highly complex and the incorporation of a company into another cannot generate any effect on the innovation rate. In other words, the acquisitions targets must have a difference between their knowledge base that able learning opportunities to be translated into new products and may even generate new technological trajectories (ClOODT and HAGEDOORN, 2006; MAKRI *et al.*, 2010). As a conclusion, in an M&A process, the relatedness of enterprises knowledge base and the innovative output are related in a form of an inverted U-shaped curve

All those studies attest that a certain amount of technological relatedness can generate opportunities for learning in areas where science plays a significant role in sustaining the innovation process. The acquisitions of firms will lead to an expansion of their knowledge base (CLOODT AND HAGEDORN, 2006), and by expanding their knowledge base, companies create new routes for research to be explored (MAKRI *et al*., 2010). In addition, multinational corporations increase their technological outputs by acquiring small enterprises with complementary capabilities (Andersen and Xiao, 2015).

Therefore, knowledge bases relatedness or any other variable that tries to measure how much of an enterprise's knowledge base is shared with its target is of extreme importance (AHUJA AND KATILA, 2001; HAGEDOORN AND DUYSTERS, 2002; DESYLLAS AND HUGHES, 2008; MAKRI *et al*., 2010). Knowledge base relatedness offers the first piece in this M&A puzzle. Based on this concept one can attest that small enterprises contribute to large enterprises through their knowledge base, depending on the degree of these relatedness the technological output will be increased.

1.2.1 Patents and patents classes as a technical element

In essence, the knowledge base relatedness is a first order condition for the success of M&As. One way of capturing part of the enterprises' knowledge is through patents (DE MATOS, 2016; NELSON AND

WINTER, 1982; NOVELLI, 2015; STRUMSKY; LOBO, 2015). Each patent is a piece of knowledge that is designed to be limited to an invention that only contains processes description (instructions) which, in theory, can be replicated from a set of basic knowledge pertaining each patent (STRUMSKY AND LOBO, 2015). For example, U.S. Patent 8,426,363, issued by Rinat Neuroscience, referred to a

> "[m]ethod for reducing a level of LDL-cholesterol by an antibody that specifically binds to PCSK9 (…) The present invention provides antagonizing antibodies, antigen-binding portions thereof, and aptamers that bind to proprotein convertase subtilisinkexin type 9 (PCSK9). Also provided are antibodies directed to peptides, in which the antibodies bind to PCSK9. The invention further provides a method of obtaining such antibodies and antibody-encoding nucleic acid. The invention further relates to therapeutic methods for use of these antibodies and antigen-binding portions thereof to reduce LDL-cholesterol levels and/or for the treatment and/or prevention of cardiovascular disease, including treatment of hypercholesterolemia." (Quoted from patent number 8,426,363, issued at USPTO in 2011)

This invention is related to a method based on molecular biology to reduce cholesterol. The full text of this patent describes the cell receptors, the DNA sequences of its antibodies and how these two elements bind. Based on this patent, companies, technologically similar to Rinat Neuroscience, could replicate the same process.

Patents by themselves are only part of what can be incorporated by a large enterprise, there is a whole set of knowledge that enabled the creation of a patent that is not shown in a patent alone (DE MATOS, 2016). A way of broadening the patent scope in terms of abilities necessary for constructing an invention is to consider the classes in which patents are classified. In a broader sense, the patent classes can give the patents technological fields and the patent breath (HALL *et al*., 2001LERNER, 1994; NOVELLI, 2015). The more classes are addressed in a patent, the larger is its breath, thus indicating a wider knowledge scope (LERNER, 1994; NOVELLI, 2015).

In sum, patent classes can summarize the technological capabilities that underlines the patent (LERNER, 1994; NOVELLI, 2015; STRUMSKY and LOBO, 2015). The patent class, in a Nelson and Winter (1982) point of view, is the domain of a knowledge neighborhood, being, then, much closer to the results of search activities than the patent alone. Therefore, patent classes are broader categories that indicate the competences needed for patenting(STRUMSKY; LOBO, 2015).

In essence, at the moment the Big-Pharma acquire a small biotech firm, the former can access the technical knowledge possessed by the small firm in the form of patents (DE MATOS, 2016).Nevertheless, incorporating this kind of knowledge, turning it on competences and routines demands learning efforts from the acquiring firm. Arguably, a small biotech company can offer to a Big-Pharmaceutical enterprise only a potential technical contribution that depends, also, on the knowledge base relatedness. In that sense, patents can show a potential contribution.

Therefore, the broader categories in which patents are classified convey an indirect indication of technical contribution, as long as it express part of the knowledge stock accumulated by enterprises. All the patents of an enterprise are the output of how it combines its technical knowledge and the combination possibilities are bounded by what the enterprise knows (AHUJA; KATILA, 2001; DE MATOS, 2016; DESYLLAS; HUGHES, 2008; HAGEDOORN; DUYSTERS, 2002).

1.3The role of scientists in the enterprises innovative activities

In large enterprises, activities may be more or less dependent on worker's skills. R&D is a typical activity that demands much from knowledge. For instance, in the pharmaceutical industry, the random screening technologies and computational models cannot build molecules by themselves; they need a trained scientist able to recognize a possible molecule (NIGHTINGALE, 2000; SCHWARTZMAN, 1976). Drug discovery is still highly dependent on the scientist skills, even in the face of a process of R&D industrialization (NIGHTINGALE, 2000; NIGHTINGALE AND MADHI, 2006). Inventors have a great effect on the enterprises technological outputs (ALMEIDA; HOHBERGER; PARADA, 2011; GRIGORIOU;

ROTHAERMEL, 2014; HOHBERGER, 2016; ZUCKER; DARBY, 2009; ZUCKER; DARBY; ARMSTRONG, 2001).

In a small enterprise, scientists are linked to the enterprise survival, which depends on the results of its scientist's research, especially among biotechnologies (COLOMBO; GRILLI, 2005; COLOMBO; PIVA, 2012; ZUCKER; DARBY, 2009; ZUCKER; DARBY; ARMSTRONG, 2001). Most times, the scientist research has enabled the firm creation (COLOMBO; PIVA, 2012). Therefore, scientists have a great role in the diffusion of these technologies in the economic environment (COLOMBO; GRILLI, 2005; COLOMBO; PIVA, 2012; OETTL, 2012; ZUCKER; DARBY, 2009; ZUCKER; DARBY; ARMSTRONG, 2001).

The firms whose workforce is composed by star scientists[1]have a higher innovation rate (ZUCKER; DARBY; ARMSTRONG, 2001). In addition, the scientist capacity to increase the enterprises innovative activity is linked to his relation towards other scientists within the same enterprise (OETTL, 2012; GRIGORIU AND ROATHERMEL, 2014). Thus, scientists allow the enterprise to have greater access to new knowledge, due to interaction with scientific community (HESS; ROTHAERMEL, 2011).

Enterprises linked to scientists who have a better reputation, regarding technologies development, are a less risky target to be acquired. Much of it is due to a certain path dependence held by scientists over their research achievements. Star scientists do not follow other star scientist research, they tend to keep researching their "own stuff" (HOHBERGER, 2016). When scientists move from one to another enterprise probably they will keep researching about the same subject they were already researching in the acquired enterprise. Therefore at the new enterprise scientists will keep researching the same "success" trajectory that has driven the acquisition.

1.3.1 Scientists as a skill element

The trajectory of the firm is built on its scientist research (HOHBERGER, 2016). The path dependence character of a research implies that the acquisition does not end a research heuristic (HOHBERGER, 2016). As scientists move from one enterprise to another, they bring with them their Skills. This type of knowledge, within the economic agents, cannot be transferred through instructions, but are acquired through learning and experience. Therefore, the workforce dedicated to research can be called as the skill knowledge set of an enterprise (Matos, 2016).

The pharmaceutical industry, despite its relationship with the patent system, depends highly on skills to innovate (Nightingale (2002); Gambardella (1995), Schwartzman (1976) and (SCHWARTZMAN; COGNAT, 1996). As skill are transferred from the small to the large company, it has impacts over the large enterprise' R&D and patent activities (ALMEIDA; HOHBERGER; PARADA, 2011; GRIGORIOU; ROTHAERMEL, 2014; HOHBERGER, 2016; OETTL, 2012; ZUCKER; DARBY, 2009; ZUCKER; DARBY; ARMSTRONG, 2001) Therefore when large enterprises acquire small firms they are trying to incorporate their skill knowledge set.

The Big-Pharma ability in retaining the core people responsible for the development of technologies is imperative and desired (DE MATOS, 2016). The people responsible for creating the patents can be a great contribution to the large pharmaceutical enterprises' R&D and patent activity. Thus, the incorporation of a skill knowledge set is a contribution that a small enterprise makes to large one. In sum, scientists are the skill part of the knowledge, being extremely important for the firms' technological outputs and these scientists can be traced through patent information

2 Methodology

[1]Zucker*et al*. (2001) definition of star scientists is based on productivity measures for articles related to genetic sequencing discoveries. For them, only 0.7% of the authors of articles, reporting genetic sequence discoveries through 1989, are star scientists.

This study will be based on the acquisitions, from 2005 to 2012, conducted by eight large pharmaceutical enterprises. The enterprises are: (i) Pfizer; (ii) Johnson & Johnson; (iii) Roche; (iv) Sanofi; (v) Astra-Zeneca; (vi) Abbott-Laboratories; (vii) Glaxo SmithKline (GSK) and (viii) Merck (that will be included only in the inventor analyses). This article deals with 8 large enterprises and 51 small enterprises

This sample will be used to construct the components in the overall contribution process. In order to understand each component one needs to: (i) explain how each component is linked to the concept of overall contribution (ii) determine how the data collected will be used and (iii) show, if necessary, how data, about large and small firms, can be combined in order to obtain correlation between agents.

The first source of data is the report "HBM PHARMA/BIOTECH M&A REPORT 2013", which compiles M&A between pharmaceutical companies and small pharmaceutical enterprises between 2005 and 2012, this report have: (i) the acquired companies, (ii) the acquiring companies and (iii) the amount spent. Based on this report the study can extracted which companies were more actively in acquiring and which spent more resources on M&A. Another important data source was the Forbes' list of the 2000 largest companies in the world[2] used as means of selecting the larger enterprises. The patents data were collected at the PatFT (Patent Full-Text and image database), a database from USPTO.

2.1 Sample definition

The sample relevancy can be attested in the following table.

Table 1: Sample Information (US$ Billions)

Companies	R&D(2012)	Total Expenses in Mergers and Acquisitions (M&A) between 2005-2013	Annual average of M&A(2005-2013)	R&D/Revenues	Annual average of M&A/Revenues	Annual average M&A/R&D
Pfizer	6,6	76,5	9,5	13%	18,60%	1,4
Johnson & Johnson	5,3	4,5	0,5	21%	2,00%	0,09
Merck&Co	8,1	2,9	0,5	17%	1,10%	0,06
Roche	14,16	48,3	6	35%	14,60%	0,4
AstraZeneca	4,4	18,3	2,2	16%	7,90%	0,5
Sanofi	5	26	3,25	12%	8%	0,65
GSK	2	8,3	1	13%	6,30%	0,5
Abbott Laboratories	4,3	4,1	0,5	11%	1,30%	0,11
Total (sample)	49,68	188,9	**23,45**	-	--	0,57
Total (world)	135	585,485	**73,18**	-	-	0,54
Total sample/Total world	37%	32%				

Source: own elaboration

The enterprises in the sample are extremely relevant for the pharmaceutical sector, these enterprises encompass 37% of the PhRMA(Pharmaceutical Research and Manufacturers of America)members expenditure in R&D. In addition, these 8 enterprises account for the 32% of all expenditures in M&A in the pharmaceutical industry.

[2] This study used the 2013 edition

2.2 Methodology for analyzing the overall contribution process

The whole article is based on the idea of Overall Contribution, which is composed by two elements, being one technical and the other skill. Technical contribution comes from techniques and therefore, patents. Skills contribution comes from the knowledge embodied in workers (in this article it has been considered the R&D workers), therefore, it comes from scientists. By uniting these two elements this article defines overall contribution as **to use the technical and skills knowledge held by the acquired small enterprise in order to build or strengthen capabilities in the acquiring enterprise.**

2.2.1 Technical contribution analyses

In order to understand how this article traces and consider the technical contribution it is necessary to raise four important points. First, this article has chosen the acquisition of small enterprises by large ones as specific phenomenon to be analyzed. Among this phenomenon, this study deals with the incorporation of biotechnologies by the Big-Pharma as a way of overcoming the productivity crises. In order to focus on biotechnologies the article will borrow the technological categories classification presented by HALL; JAFFE; TRAJTENBERG (2001). Then, biotechnologies will be all the patent subclasses encompassed by the classes 435 and 800.

Second, patents have two important properties: (i) they can be used to generate new patents (HALL; JAFFE; TRAJTENBERG, 2001; TRAJTENBERG; HENDERSON; JAFFE, 1997) (ii) the patent classes conveys the capabilities necessary for the production of patents with certain characteristics (LERNER, 1994; NOVELLI, 2015; STRUMSY and LOBO, 2015). Thus, the patent classes dominated by an enterprises can show their technical knowledge set.

Third, when a small firm is acquired the large enterprise, the later has access to the former knowledge set and products, in this case, the patents. But, the successful incorporation and use of the small enterprises knowledge set is not assure this process depends on the large enterprises' ability to cope up with the small enterprise contribution. As discussed here, much of the technical knowledge's successful incorporation depends on the knowledge base relatedness.

Finally, the proposed line of though here say that the enterprises' knowledge bases start with some degree of relatedness that may grow over the years, this means that large pharmaceutical enterprises that are building competences close to the ones held by the small enterprises are, somehow, exploring the small enterprises technical knowledge set.

Technical contribution, then, can be divided in two. Large enterprises can use the small enterprises patents to generate new patents (direct way) or the large enterprises can use the small enterprises technical knowledge to patent in new classes or increase its patent activities in already developed classes or competences (indirect way).

The direct use of small enterprises technical knowledge can be seen by searching the small enterprises patents used as reference in the large enterprises patents (HALL; JAFFE; TRAJTENBERG, 2001; TRAJTENBERG; HENDERSON; JAFFE, 1997). In addition, the direct use of patents can be combined with citation lags. The citation lag is the distribution of patent citation over the years, this lag was calculated by HALL; JAFFE; TRAJTENBERG, (2001) in their study bout the USPTO database for methodological approach. The authors used the same database as the study that is why this citation can be used here.

The indirect form of contribution requires compiling the small enterprises' knowledge set. This is done by gathering patent class and subclasses that compose the small enterprises patent universe. As the technical knowledge set is defined, the correlation is built by gathering when the large enterprise started to apply its first patent in each of classes.

The technical contribution analyses is way to observe the use of technical knowledge made by large enterprise. In sum, it shows an evolution process of competence development and creation. By doing this one can observe when the acquiring company began to incorporate new classes and subclasses to its technical knowledge set.

2.2.2 Skill contribution

Patents are only a partial amount of knowledge available for the enterprises that engage in acquisitions. Patents as techniques are “inherited” in the acquisition process. Nevertheless, the scientists that work in an enterprise are another important source of knowledge.

On one hand, the technological knowledge described in a patent is very specific and has a particular purpose, as can be seen in the example of patent No. 8,426,363 (see pg. 6). On the other hand, skills have a characteristic of being more "elastic" and "amorphous", they can be considered less rigid because they can be applied in similar technological elements. The greater "flexibility" held by skills allows scientist to employ them in similar research subjects that will lead to different kind of drugs. Nevertheless, the drug purposes should not be so distinguished. The same scientist can work in a series of researches that encompass the same mechanism such as inhibition of a cell receptor. Arguably, inhibiting a cellular receptor has the same principle, no matter if this receptor is responsible for kidney or liver enzymes. Yet, technical knowledge, as patent 8,426,363, cannot be applied to anything other than what it describes. In contrast, skills embodied in agents can be allocated in similar research and development processes (DE MATOS, 2016)

These type of knowledge that is embedded in workers are broad. Arguably, all workers in an enterprise have a certain level of skills. In an attempt to reduce this broadness and, therefore to have a better *proxie* for skills, this research considers only R&D. Another important element to be considered in considering the skills in the small enterprises is this kind of firms has just a few employees and patents. Therefore, the people identifie in the patents as inventors may represent the core of skills in a small enterprise, so skills have as *proxie* the inventors presented in the patent description. Therefore, the skill set is defined in this study as all the inventors compiled through the company’s patents. In order to track the skill contribution of a small company to a large company, this study, seeks which inventors has changed from the small acquired small company to the large acquiring enterprise

Table 2: MethodologySummary Table

Overall contribution component	**Key elements**	**Data source**
Direct technological contribution	Patents used as reference	Patents Reference
Indirect technological contribution	Technical knowledge set analyses	Patents applied in new classes
Skills Contribution	Skill set analyses	Patent inventors

Source: Own elaboration

The methodology can be summarized in the table above. There are all the overall contribution elements and their data sources.

3. Data Analyses

3.1 Technical contribution analyses

The technical contribution traces all the techniques expressed though patents that could contribute to the large enterprises technological development. The following table shows the number of patents of each enterprise, which was used as reference in new patents.

Table 3: Direct technical contribution

Large enteprises	Enterprises acquired	Number of small enteprises patents	Patents used as reference (small enteprise's patents used)	Patents generated
Astra Zeneca	Kudos	30	5	3
	Medimmune	347	1	4
	Novexel	6	3	1
Sanofi	Fovea	5	1	1
	VaxDesign	24	3	1
GSK	Human Genome Science	711	14	9
	ID Biomedical	48	3	5
	Corixa	50	33	20
	Praecis	44	3	2
	Sirtirs	14	9	5
Pfizer	Idun Pharmaceuticals	39	1	1
	Rinat Neuroscience	27	2	3
	Coley	56	34	7
	Covx	8	1	3
	Incagen	91	2	1
J&J	Transform-Pharma	28	1	10
	Omrix	26	6	12
Merck	Sirna (Ribozyme)	192	35	32
	Glycofi	40	26	9
	Abmaxis	6	5	1
	Inspire	96	1	1
Roche	Piramed	4	4	13
	Arius	35	5	11
	Mirus-bio	37	12	7

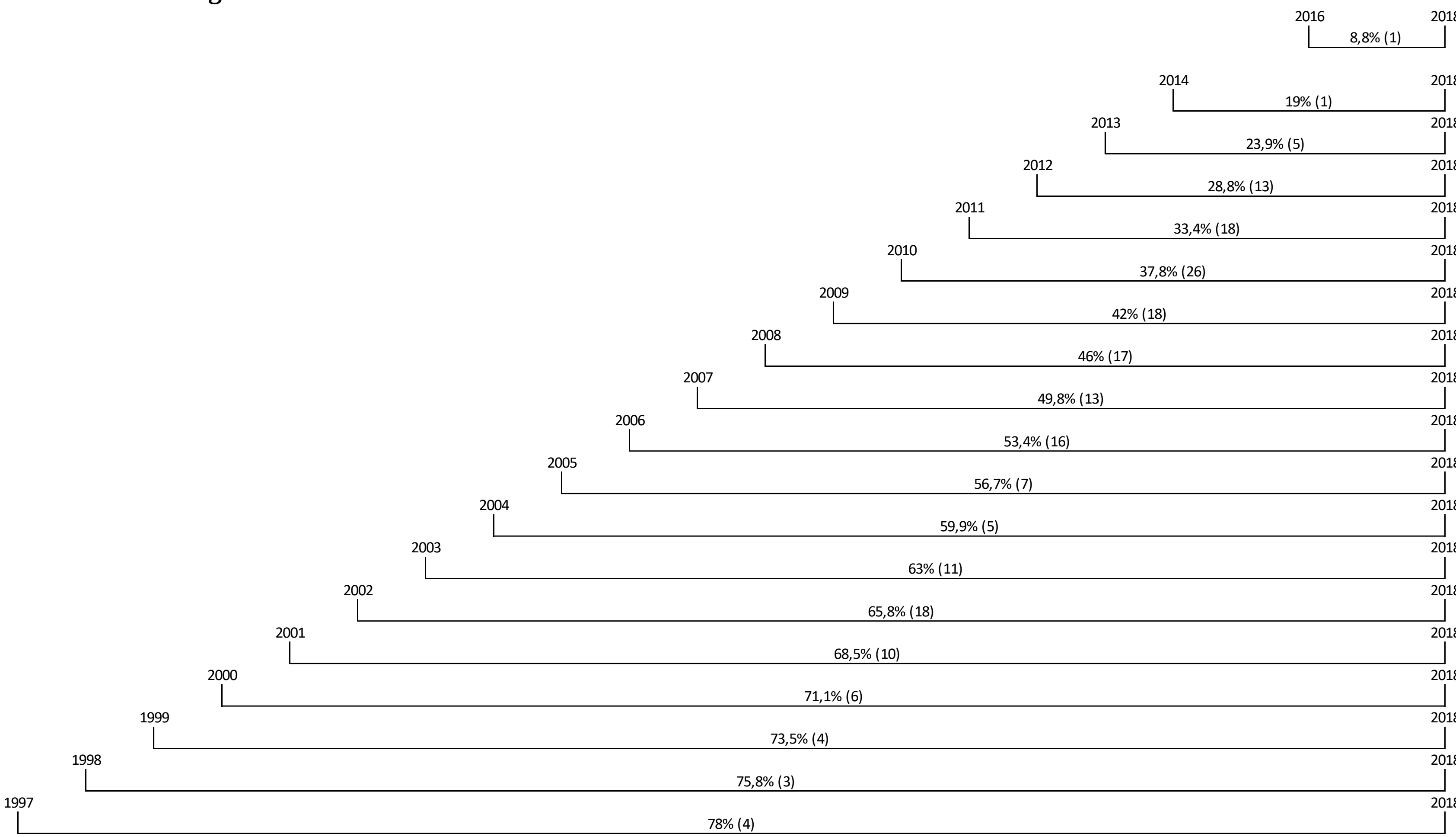
Source: Own Elaboration

Table 3 shows that large enterprises tend not to use patents from all the acquired enterprises. Even fewer small enterprises have half of their patents referenced by large enterprises.

In terms of outcomes, the enterprises that have at least one of their patents referenced, just a small share of each enterprise's patents have generate other patents. Of course, these patents can be highly relevant, but they are just a small number when one compares to all of the small enterprises patents.

One way of picturing the patents relevancy is to analyze their citation lag. This lag indicates, in percentage, the amount of citations a patent have, according to the year the patent was granted. Patents may depreciate over the years leading to lesser rate of citations. As a general pattern, new patents have a lager potential of being cited. Therefore, large enterprises can inherit patents that are going to be cited (new patents) and patents that are old and its citing potential are diminished, the citation lag tries to identify that (HALL; JAFFE; TRAJTENBERG, 2001). Picture 1 uses the citation lag proposed by HALL; JAFFE; TRAJTENBERG (2001). In picture is compiled all patents filled by the small acquired enterprise that were referenced by the large enterprises, at its left side is the year in which the patent was granted, at the right side is end of the period that is 2018. In the middle of the picture is the percentage of citations that the enterprises have. According to the citation lag, for example the patent that was granted in 1997 have had 78% of all citations possible. In parentheses are the number of patents granted in the year and cited by the large enterprise, for example that are only 4 patents granted in 1997 that was cited by a large enterprise.

Picture 1: Citation Lag



In total, the large enterprises have cited 196 patents from the small acquired enterprises. In order to have a better comprehension about the patent potentiality one can divide the 196 patents in tiers. Being the first tier the patents that have had from 0% to 25% of its citation. The second tier are the patents that have had from 25% to 50% of tis citations. The third tier encompass patents that have had from 50% to 75% of its citations and the last tier are the patents that have had from 75% to 100% of its citations. In other words, the patents in the first tier are the ones that have a greater potential and the patents in the last tier have a lower potential.

Table 4: Patent potentiality divided in tiers

Tier in percentage	Number of patents
0-25	7
25-50	110
50-75	77
75-100	7

Source: Own elaboration

The majority of patents are the ones that have had form 25% to 75% of all possible citations. One can break this tier into more the tiers, in order to have a better look over the patents. The new tiers are from: (i) 25%-40%; (ii) 40%-55%; (iii) 55-75%.

Table 5: More potential tiers

Tier in percentage	Number of patents
25-40	57
40-55	76
55-75	59

Source: Own elaboration

This division shows that there is no clear majority, but a greater number of patents have had from 40% to 55% of all possible citations. The citation lag data shows that the patents held by the large enterprises still have a good potential to generate new patents. Nevertheless the "productivity" of patents, i.e the number of patents generated, is low. In most cases, the large enterprises generate less patents than the amount used. This fact indicates that small enterprises' patents are extremely specific and were not used in broad array of possibilities. Therefore, these patents are a small piece of a greater technical knowledge. As consequence, small enterprise patent by itself cannot produce several new inventions, this characteristic indicates that these patents are used to fill or enhance some technologies that are being developed and not that these elements have the potential to initiate new trajectories within the large enterprise.

Technical contribution can also be understood in an indirect way, as a potentiality. Indirect technical contribution can be characterized as potential because for being fulfilled it depends on the large enterprises' ability and commitment for developing the same competences held by the small enterprise. For instance, the acquired small enterprise may have patents in several classes that are not encompassed by the large enterprise' patents, but this means that the Big-Pharma will only develop this classes by creating patents covered by if they chooses to do so.

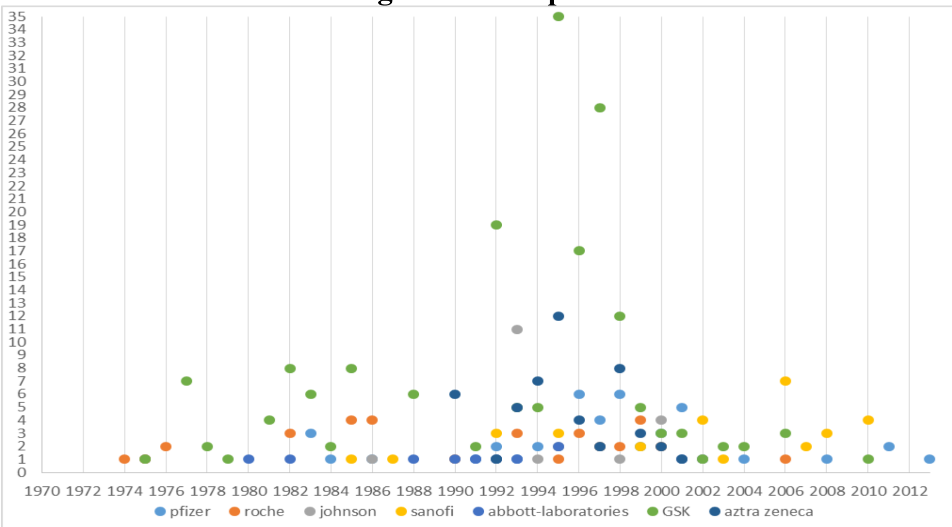
Another important aspect is to consider that the Big-Pharma uses the small acquired enterprises to further developed patent classes whose development started internally and some time ago. This aspect is highly related to the process of biotechnologies diffusion (HOPKINS et al., 2007, 2013; NIGHTINGALE; MARTIN, 2004; SHARP, 1996)

The process of further developing patent classes is a process of creating absorptive capabilities, by doing that, the Big-Pharma becomes aware of new technological developments. In addition, the increasing understanding about general principle of some technology allows to choose better suited techniques for the enterprise(COHEN; LEVINTHAL, 1990).

The graphic1 contains the indirect technical contribution analyses. In the Y axis is shown the number of new classes developed. A new class is the first time the large enterprise has filed a patent in a patent subclass that it has not before. In the X axis the years are represented. For example, in 1994 GSK has started to patent in five new classes.

The classes and subclasses being considered are the ones that compose the small enterprises technical knowledge set. Therefore, this graphic presents a correlation between the knowledge developed be the small enterprises and how, though the years, this knowledge was developed by the Big –Pharma that acquired the small firms.

Graphic1: Big-pharma's technical Knowledge set development



Source: Own elaboration

Through the graphic above one can draw a pattern for technological development. At a first glance, almost all the large enterprises have intensified their development over the small enterprises' technical knowledge from 1992 onwards. Before 1992 the development of new classes is scare and it happens just in few enterprises.

This process, after 1992, has some important aspects. The development of subclasses related to biotechnologies is new but it does not started with acquisitions analyzed. This behavior indicates that biotechnology "follows a well-established, historical pattern of slow and incremental of technological diffusion"(Nightingale and Martin, 2004, pg. 564) in which new technology is being incorporated gradually to large pharmaceutical companies (ZUCKER; DARBY, 1997).

Based in graphic 1, the technical contribution of small enterprises allows the Big Pharma to further developed elements that it has started in the past. The great majority of classes were developed before the acquisition of these enterprises. Not only that, but these enterprises were acquired at the moment the development of new classes are losing its pace, from 2005 to 2012.

One way of observing the process of technical contribution and its exhaustion is to see the percentage of the small enterprises technical knowledge set that was not developed. For instance, if he Big-Pharma has already developed a large portion of the small enterprises technical knowledge set, this same small enterprise can contribute much less, technically, into creating new competences in the large enterprise. A large portion of the contribution, in this case, will be linked to enhancing already existent competences

Table 6: The portion of not developed technical knowledge set

Technical Knowledge not developd	
Enterprise	Percentage
J&J	66%
Astra-Zeneca	32%
Abbott-Labrotories	27%
GSK	14%
Pfizer	12%
Roche	10%
Sanofi	6%

Source: own elaboration

Table 6 shows the technical contribution exhaustion. The low percentage of not developed patent classes mean that are few opportunities for creating new competences. But, still, there is the possibility of further developing existent classes, this fact shed light on the features of the technical contribution as a contribution for further developing competences and not creating new ones.

3.2 Skill Knowledge Analyses

The other important element for this article is the skills contribution, as mention before, the skills are the knowledge embedded in the agents that, in this case, are dealing with R&D. Therefore, when large enterprises acquire small firms the large ones can keep the key people dedicated to the R&D and, thus, keep the skills.

The skills contribution is rather simple. This article observes the inventors that were incorporated by the large enterprise, this can be seen by looking at the patent inventors. First, inventors, that had at least one patent under the small acquired enterprises, were compiled. This group of inventors was called skill knowledge set. After establishing the skill knowledge set, the article searches which inventor has at least filled one patent having the acquiring Big-Pharma as assignee. Therefore, one can stablish a relation called inventors use, being it the percentage of the acquired small enterprises skill knowledge that was used by the large enterprise. The following tables summarize the findings

Table 7: Skill contribution summary table

	Small acquired enterprises	Total of inventoris in the acquired companies (B)	Inventors that started to patent by Pfizer (C)	Use of Inventors (C/B)
Pfizer	Rinat Neurosicence	35	18	51%
	Encysive	25	8	32%
	Coley	61	9	15%
	Vicuron	47	6	13%
	Icagen	68	8	12%
	Idun Pharmaceuticals	25	0	0%
	Biorexis	5	0	0%
	CovX	27	0	0%
	Serenex	25	0	0%
	FoldRx	3	0	0%
	Excaliard	8	0	0%
Roche	Piramed	24	24	100%
	Mirus-Bio	25	19	76%
	Arius	14	5	36%
	Therapeutic Human Polyclonals	4	0	0%
	Memory Pharmaceuticals	26	0	0%
	Macardia	2	0	0%
Abbott-Laobratories	Facet-Biotech	30	18	60%
	KOS-Pharmaceuthicals	14	1	7%
J&J	TransForm Pharmaceuticals	33	8	24%
	Crucell	81	1	1%
	Omrix	22	0	0%
	Respivert	15	0	0%
	Corimmun	5	0	0%
Merck	Glycofi	13	10	77%
	Abmaxis	10	6	60%
	Sirna (Ribozyme)	112	12	11%
	Inspire	80	3	4%
	Insmed	27	1	3%
	Novacardia	5	0	0%
	Smartcells	8	0	0%
Sanofi	VaxDesign	28	28	100%
	Acambis (ex Peptide Therapeutics)	30	12	40%
	Fovea	6	2	33%
	Zentiva	42	0	0%
	BiPar Sciences	12	0	0%
	TargeGen Inc.	19	0	0%
Astra-Zeneca	Novexel	21	7	33%
	Kudos	52	10	19%
	Medimmune	105	3	3%
	Cambridge Antibody Technology	45	0	0%
	Arrow Therapeutics	10	0	0%
	Ardea Biosciences	34	0	0%
	Pearl Therapeutics	8	0	0%
GSK	Reliant Pharmaceuticals	3	2	67%
	Praecis	75	18	24%
	Domantis	41	6	15%
	Corixa	124	17	14%
	ID Biomedical	46	5	11%
	Cellzome	41	4	10%
	Genelabs Techn.	101	3	3%
	Human Genome Science	214	3	1%
	Stiefel Laboratories	35	0	0%

Source: Own elaboration

The skills contribution are relevant when one considers the group of acquired enterprises. All large enterprises have used skills of the acquired small firms. From all acquired enterprises at least 40% of them have contributed in skills. Individually some enterprises have contribute with 100% of their skills.

To keep key personal inside is one important objective of the Big-Pharma (DE MATOS, 2016). Therefore, skills are seen as advantage for the large enterprise for internalizing the relevant research done in the small enterprise, mainly due to the scientist path dependence (HOHBERGER, 2016).

One important relation stands out when one analyses together the classes not developed and skills contribution. The enterprises with a higher rate of non-developed classes are the ones that have used the lesser amount of inventor, for instance, the case of J&J that have 66% of not developed classes and a low inventors usage. This fact may lead to an important relation. The inventors are the ones responsible for developing new technologies, therefore the more a inventors is used the more a large enterprise can develop the same competences and enhance the competences in accordance to the technical contribution of the small acquired enterprise. Thus, the effective use of technical contribution depends on the level of skill contribution.

Conclusion

This article was an attempt to show what elements are kept by the large enterprises when it acquire small firms. In order to that, this study was based on the M&A data between Big-Pharma and Small pharmaceutical enterprises from 2005 to 2012.

The first step taken was to establish that small enterprises can contribute to large enterprises increasing their innovative outputs. This article divided the contribution in two main elements: the technical and skill contribution. Both of it have different sources. Technical contribution comes from the techniques developed by the small enterprises and skill contribution comes from the workers that deals with R&D. By uniting these two elements one can define this whole process as overall contribution.

Therefore, the elements incorporated by Big-Pharma whose origin are the small firms can be traced though the analyses of the technical and skill knowledge. The technical contribution analyses is composed by the patents used as reference by the large enterprises and how the large enterprise' knowledge set has become more similar to the one held by the small enterprises. This process encompass compiling when the large enterprise started to file patents on the same patent classes dominated by the small enterprises. As a conclusion, this study observed that the technical contribution was not used to create new competences, but it was used to improved already developed competences.

The skill contribution analyses was conducted by observing if the small enterprises' inventors started to file patent for the large acquiring enterprise. As a conclusion, this study state that skills are used much more extensively than techniques, being it more prominent among the elements incorporated.

Bibliographic References

ACHILLADELIS, B.; ANTONAKIS, N. The dynamics of technological innovation : the case of the pharmaceutical industry. 2001.

AHUJA, G.; KATILA, R. Technological Acquisition and the Innovation Performance of Acquiring Firms: A Longitudinal Study. **Strategic Management Journal**, v. 22, n. 3, p. 197–220, 2001.

AHUJA, G.; LAMPERT, C. M. Entrepreneurship in the large corporation: A longitudinal study of how established firms create breakthrough inventions. **Strategic Management Journal**, v. 22, n. 6–7, p. 521–543, 2001.

ALMEIDA, P.; HOHBERGER, J.; PARADA, P. Individual scientific collaborations and firm-level innovation. **Industrial and Corporate Change**, v. 20, n. 6, p. 1571–1599, 2011.

ANDERSSON, M.; XIAO, J. Acquisitions of start-ups by incumbent businesses: A market selection process of "high-quality" entrants? **Research Policy**, v. 45, n. 1, p. 272–290, 2016.

BAUER, F. et al. Mergers and Acquisitions , Entrepreneurship and Innovation Article information : 2016.

CARTER, P. H. et al. Investigating investment in biopharmaceutical R&D. **Nature Reviews Drug Discovery**, v. 15, n. 10, p. 673–674, 2016.

CASSIMAN, B.; VEUGELERS, R. Are external technology sourcing strategies substitutes or complements: The case of embodied versus disembodied technology acquisition. v. 3, n. 672, p. 1–22, 2007.

CHAKRABARTI, A., HAUSCHILDT, J., SUVERKRUP, C. Does it pay to acquire technological firms? In: R&D Management, 24, pg. 47-56, 1994

CLOODT, M.; HAGEDOORN, J.; VAN KRANENBURG, H. Mergers and acquisitions: Their effect on the innovative performance of companies in high-tech industries. **Research Policy**, v. 35, n. 5, p. 642–654, 2006.

COHEN, W. M.; LEVINTHAL, D. A. Absorptive Capacity : A New Perspective on and Innovation Learning.

Administrative Science Quarterly - Special Issue: Technology, v. 35, n. 1, p. 128–152, 1990.
COLOMBO, M. G.; GRILLI, L. Founders' human capital and the growth of new technology-based firms: A competence-based view. **Research Policy**, v. 34, n. 6, p. 795–816, 2005.
COLOMBO, M. G.; PIVA, E. Firms' genetic characteristics and competence-enlarging strategies: A comparison between academic and non-academic high-tech start-ups. **Research Policy**, v. 41, n. 1, p. 79–92, 2012.
COMANOR, W. S.; SCHERER, F. M. Mergers and innovation in the pharmaceutical industry. **Journal of Health Economics**, v. 32, n. 1, p. 106–113, 2013.
DE MATOS, M. M. **CHANGES IN INNOVATION DYNAMICS OF THE PHARMACEUTICAL INDUSTRY :** [s.l.] Tese, 2016.
DESYLLAS, P.; HUGHES, A. Sourcing technological knowledge through corporate acquisition: Evidence from an international sample of high technology firms. **Journal of High Technology Management Research**, v. 18, n. 2, p. 157–172, 2007.
DESYLLAS, P.; HUGHES, A. Do high technology acquirers become more innovative? **Research Policy**, v. 39, n. 8, p. 1105–1121, 2010.
DIMASI, J. A. New Drug Innovation and Pharmaceutical Industry Structure: Trends in the Output of Pharmaceutical Firms. **Drug Information Journal**, v. 34, n. 4, p. 1169–1194, 2000.
EJERMO, O.; XIAO, J. Entrepreneurship and survival over the business cycle: How do new technology-based firms differ? **Small Business Economics**, v. 43, n. 2, p. 411–426, 2014.
GAMBARDELLA, A. Science and Innovation: The U.S. Pharmaceutical industry During the 1980's, Cambridge University Press, Cambridge, 1995.
GERPOTT, T. J. Successful integration of R&D functions after acquisitions: An exploratory empirical study. **R&D Management**, v. 25, n. 2, p. 161–178, 1995.
GLEADLE, P. et al. Restructuring and innovation in pharmaceuticals and biotechs: The impact of financialisation. **Critical Perspectives on Accounting**, v. 25, n. 1, p. 67–77, 2014.
GRABOWSKI, H. G.; VERNON, J. M. Returns to R&D on new drug introductions in the 1980s. **Journal of Health Economics**, v. 13, n. 4, p. 383–406, 1994.
GRABOWSKI, H. G.; VERNON, J. M. The determinants of pharmaceutical research and development expenditures. **Journal of Evolutionary Economics**, v. 10, p. 201–215, 2000.
GRIGORIOU, K.; ROTHAERMEL, F. T. Structural Microfoundations of Innovation: The Role of Relational Stars. **Journal of Management**, v. 40, n. 2, p. 586–615, 2014.
HAGEDOORN, J.; DUYSTERS, G. The Effect of Mergers and Acquisitions on the Technological Performance of Companies in a High-tech Environment. **Technology Analysis & Strategic Management**, v. 14, n. 1, p. 67–85, 2002a.
HAGEDOORN, J.; DUYSTERS, G. External sources of innovative capabilities: The preference for strategic alliances or mergers and acquisitions. **Journal of Management Studies**, v. 39, n. 2, p. 167–188, 2002b.
HALL, B. H.; JAFFE, A. B.; TRAJTENBERG, M. **THE NBER PATENT CITATIONS DATA FILE: LESSONS, INSIGHTS AND METHODOLOGICAL TOOLSNo Title**: Working paper 8498. [s.l: s.n.].
HESS, A.; ROTHAERMEL, F. T. WHEN ARE ASSETS COMPLEMENTARY? STAR SCIENTISTS, STRATEGIC ALLIANCES, AND INNOVATION IN THE PHARMACEUTICAL INDUSTRY. **Strategic Management Journal**, v. 32, p. 8950909, 2011.
HOHBERGER, J. Does it pay to stand on the shoulders of giants? An analysis of the inventions of star inventors in the biotechnology sector. **Research Policy**, v. 45, n. 3, p. 682–698, 2016.
HOPKINS, M. M. et al. The myth of the biotech revolution: An assessment of technological, clinical and organisational change. **Research Policy**, v. 36, n. 4, p. 566–589, 2007.
HOPKINS, M. M. et al. Buying big into biotech: Scale, financing, and the industrial dynamics of UK biotech, 1980-2009. **Industrial and Corporate Change**, v. 22, n. 4, p. 903–952, 2013.
HUSSINGER, K. On the importance of technological relatedness: SMEs versus large acquisition targets.

Technovation, v. 30, n. 1, p. 57–64, 2010.
LAURSEN, K.; SALTER, A. J. The paradox of openness: Appropriability, external search and collaboration. **Research Policy**, v. 43, n. 5, p. 867–878, 2014.
MAKRI, M.; HITT, A.; LANE, P. Complementary Technologies, Knowledge Relatedness and Invention Outcomes in High Technology Mergers and Acquisitions. In: Strategic Management Journal, 31, pp. 602-628, 2010.
MAKRI, M.; LANE, P. J. Responding to technological maturity: A socio-cognitive model of science and innovation in technological communities. **Journal of High Technology Management Research**, v. 18, n. 1, p. 1–14, 2007.
MALERBA, F.; ORSENIGO, L. The evolution of the pharmaceutical industry. **Business History**, v. 57, n. 5, p. 664–687, 2015.
MUNOS, B. Lessons from 60 years of pharmaceutical innovation. **Nature reviews. Drug discovery**, v. 8, n. 12, p. 959–968, 2009.
NIGHTINGALE, P. Economies of scale in experimentation: knowledge and technology in pharmaceutical R&D. **Industrial & Corporate Change**, v. 9, n. 2, p. 315, 2000.
NIGHTINGALE, P.; MARTIN, P. The myth of the biotech revolution. **Trends in Biotechnology**, v. 22, n. 11, p. 564–569, 2004.
NORBÄCK, P.; PERSSON, L. Born to be global and the globalization process. 2013.
NOVELLI, E. An examination of the antecedents and implications of patent scope. **Research Policy**, v. 44, n. 2, p. 493–507, 2015.
OETTL, A. Reconceptualizing stars: Scientist helpfulness and peer performance. **Management Science**, v. 58, n. 6, p. 1122–1140, 2012.
PAUL, S. M. et al. How to improve R&D productivity: the pharmaceutical industry's grand challenge. **Nature reviews. Drug discovery**, v. 9, n. 3, p. 203–14, 2010.
PENROSE, Edith T. The theory of the growth ofthe firm. **New York: Sharpe**, 1959.
POWELL, W. W. et al. the Life Sciences Network Dynamics and Field Evolution : The Growth of Interorganizational Collaboration in the Life Sciences 1. **American Journal of sociology**, v. 110, n. 4, p. 1132–1205, 2013.
POWELL W.W. KOPUT, K. W. S.-D. L. Collaboraation and the locus of innovation: networks of learning in biotechnology. **Administrative Science Quarterly**, v. 41, n. 1, p. 116–145, 1996.
QUÉRÉ, M. The post-genome era: rupture in the organization of the life science industry? In: McKELVEY, M., RICKNE, A., LAAGE-HELLMAN, J. The Economic Dynamics of Modern Biotechnology, Edward Elgar, Northhampton, USA, 2004
SCHWARTZMAN, D. Innovation in the Pharmaceutical Industry, The Johns Hopkins university Press, Baltimore, Maryland, 1976
SCHWARTZMAN, D.; COGNAT, A. Has Pharmaceutical Research Become More Scientifk ?. 1996.
SCHWEIZER, L. Organizational integration of acquired biotechnology companies into pharmaceutical companies: The need for a hybrid approach. **Academy of Management Journal**, v. 48, n. 6, p. 1051–1074, 2005.
SHARP, M. STEEP Discussion Paper No 28 The Science of Nations : European Multinationals and American Biotechnology. v. 44, n. 28, 1996.
STRUMSKY, D.; LOBO, J. Identifying the sources of technological novelty in the process of invention. **Research Policy**, v. 44, n. 8, p. 1445–1461, 2015.
SZÜCS, F. M&A and R&D: Asymmetric Effects on acquirers and targets? **Research Policy**, v. 43, n. 7, p. 1264–1273, 2014.
TRAJTENBERG, M.; HENDERSON, R.; JAFFE, A. University Versus Corporate Patents: A Window On The Basicness Of Invention. **Economics of Innovation and New Technology**, v. 5, n. 1, p. 19–50, 1997.
XIAO, J. **Ownership Change , Multinationals , and Growth of New Technology - Based Firms Ownership**

Change , Multinationals , and Growth of New Technology - Based Firms. [s.l: s.n.].
XIAO, J. The effects of acquisition on the growth of new technology- based firms : Do different types of acquirers matter ? **Small Business Economics**, p. 487–504, 2015.
ZUCKER, L. G.; DARBY, M. R. Present at the biotechnological revolution: transformation of technological identity for a large incumbent pharmaceutical firm. **Research Policy**, v. 26, n. 4–5, p. 429–446, 1997.
ZUCKER, L. G.; DARBY, M. R. Star Scientists, Innovation and Regional and National Immigration. **Entrepreneurship and Openness Entrepreneurship and Openness Theory and Evidence**, 2009.
ZUCKER, L. G.; DARBY, M. R.; ARMSTRONG, J. S. COMMERCIALIZING KNOWLEDGE: UNIVERSITY SCIENCE, KNOWLEDGE CAPTURE, AND FIRM PERFORMANCE IN BIOTECHNOLOGY. **NBER Working Paper Series**, n. Working Paper 8499, 2001.