IV ENEI
Encontro Nacional de Economia Industrial e Inovação
Inovação, Produtividade e os Desafios do Crescimento
10 a 12 de setembro de 2019
Campinas, São Paulo

Interaction between Big-Pharma's and Small Enterprises: an Analyses Focused on the Incorporation of Inventors.

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Area Tematica: 3.3 Estratégias Empresariais

JEL: O31, L26

Resumo: O artigo foca na incorporação de conhecimento pela grande empresa farmacêutica em processos de aquisição de pequenas empresas. O objetivo é identificar em que grau a incorporação do conhecimento relacionado aos inventores é efetivada nesse processo. Usa-se uma metodologia qualitativa, que parte de uma amostra de grandes empresas farmacêuticas e as pequenas empresas adquiridas por elas no período de 2005 a 2012. A partir da amostra compilou-se as patentes concedidas às pequenas empresas junto ao USPTO, por meio da base PatFT. A análise desenvolve duas medidas centrais. A primeira é o uso de inventores definida como os inventores das pequenas que ao serem incorporados passam a patentear pela grande empresa. A outra é a incorporação de trajetórias de pesquisa entendido como os inventores que citam seu trabalho passado à medida que são incorporados à grande empresa. Conclui-se que as grandes empresas incorporam inventores de pelo menos uma das empresas adquiridas, porém o número de inventores incorporados é relativamente baixo. Mais rara é a incorporação de trajetórias de pesquisa que, por isso, demonstram sua relevância.

Palavras-chave: Aquisição, Indústria Farmacêutica, Pequenas Empresas, Patentes

Abstract: This article focuses on the incorporation of knowledge by the Big-Pharma as it acquire small enterprises. The objective is to identify in which degree the incorporation of the knowledge, related to the inventors, is effected in this process. Through a qualitative methods, based on a sample of Big-Pharmas and small companies acquired by them from 2005 to 2012 we compile the patents granted to small companies within the USPTO, through the base PatFT. The analysis develops two central measures. The first is the use of inventors defined as small enterprises' inventors that were incorporated and start to develop patents for the large enterprise company. The other is the incorporation of research trajectories meaning inventors who cite their past work as they are incorporated into the larger enterprise. It is concluded that large companies incorporate inventors of at least one of the acquired companies, but the number of incorporated inventors is relatively low. More rare is the incorporation of research trajectories that, therefore, demonstrate their relevance.

Keywords: Acquisitions, Pharmaceutical Industry, Small Enterprises, Patents

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Introduction

The technological dynamics in the pharmaceutical R&D is underpinned on its increasing complexity. This process obliges the enterprises to cope up with different competences and technologies outside its knowledge base and, of course, its boundaries (Gambardella, 1995; Gassmann, *et. al.*, 2005; Martin; *et. al.*, 2008; Nightingale, 2000). This study focus on that process by analyzing the incorporation of inventors by large pharmaceutical enterprises through the acquisition of small enterprises.

The interest in analyzing this particular interaction between large and small enterprises derives from the fact that, nowadays, new technologies are increasingly being developed within small firms which, generally, span out from the academic environment (Almeida, Hohberger, Parada, 2011; Colombo, Piva, 2012; Author, 2016[1]; Hohberger, Almeida, Parada, 2015; Powell *et. al.*, 2005). As such, small enterprises are seen as complementary to the large enterprises' R&D (Cassiman; Veugelers, 2007) and the former become compelled to interact in order to successfully conduct research activities (Baumol, 2002).

Acquisitions are one of the main forms of interaction identified in the literature (Comanor and Scherer, 2013; Gleadle *et. al.*, 2013; Hopkins *et. al.,* 2013; Light and Lexchin, 2012; Hopkins *et. al.* 2012; Higgins and Rodriguez, 2006; Munos, 2009; Paul *et. al.,* 2010). Several studies have tried, in different degrees, to address the reasons and outcomes of this process. They have shed light on the correlation between acquisitions and enterprises innovative outputs (Ahuja; Katila, 2001; Andersson; Xiao, 2016; Gerpott, 1995; Granstrand, 2000; Granstrand *et. al.*, 1992; Desyllas, Hughes, 2007, 2010 Hagedoorn; Duysters, 2002; Norbäck; Persson, 2013; Xiao, 2015).

These sectoral, but broad studies, carry with them some problems. Although, the correlation between acquisition and innovative output is proved, this process, broadly named as knowledge incorporation, is multifaceted and unfortunately underestimated. This problem can be decreased by an analyses focused on specific elements, or variables, that improve enterprises innovative outputs.

From the many sides encompassed by the knowledge incorporation, one of them, and the focus of this study, is the incorporation of inventors enabled by acquisitions. Therefore, this article objective is to evidence in which degree inventors and, consequently, embedded knowledge is incorporated by a sample of 8 large pharmaceutical enterprises. In order to do this, we will set two methodological steps. The first is to define and

[1] In order to avoid the authors identification all self citations were substituted for the form Author (year).

observe the incorporation of inventors. This will be done by compiling the inventors of the small target enterprise that started to patents for the acquirer large enterprise. The second is to define and observe evidence of the incorporation of inventor's research trajectory. This step encompass compiling the inventors that cite their own patents in different enterprises, in other words, inventors that reference their past work as they move from the target to the acquirer enterprise.

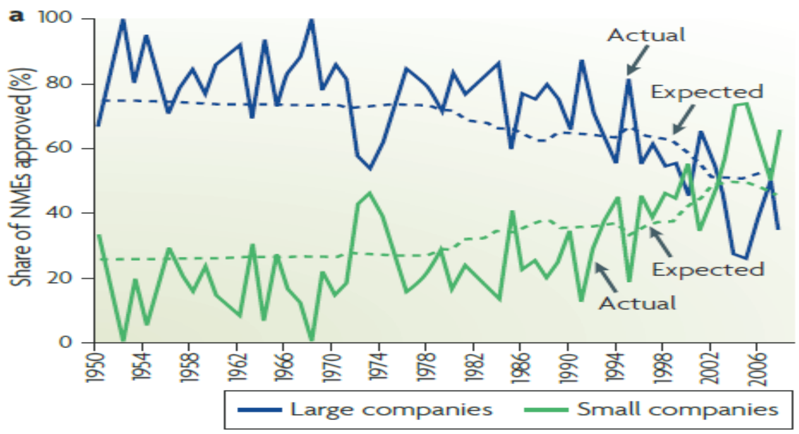
On one hand, if this study point that Big-Pharma **do not** incorporate the inventors in its routines we are evidencing that technology can be understood regardless of its creator. On the other hand, by showing that inventors are incorporated in enterprises routines we will evidence the importance of embedded knowledge. Then we can advance to the second step methodological step and show a research trajectory incorporation. By identifying this process, this article will be looking to a very interest phenomenon of incorporating research done outside the large enterprise borders. Therefore, looking at the same variable we can identify two processes. In the end we will be reassuring inventors as an important source of knowledge in enterprises.

This article is composed by 4 sections and a conclusion. The first section discusses the importance of small enterprises in the pharmaceutical industry output and the increasing number of acquisitions of small enterprise by Big-Pharma. The second section will discuss the inventor and his impact on small enterprises' innovativeness. The third section presents the methodology. The fourth section encompasses the results and discussion and then the conclusion is presented.

1 The growing importance of small enterprises and the incorporation of new competences

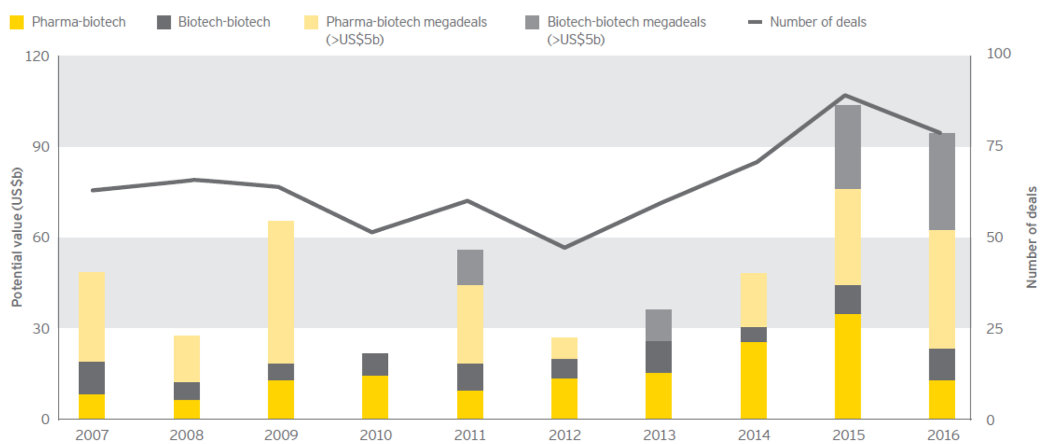
Nowadays, the share of innovative output of small enterprises is growing, making them a relevant actor in the industry (see figure 1, pg. 11). Furthermore, the large pharmaceutical enterprises have improved their interaction with small enterprises by creating scouting teams dedicated only to search for promising new technologies developed by small enterprises (AUTHOR, 2016). Impressively, 50% of large enterprise's new technologies were originated in small enterprises (AUTHOR, 2016). In this context, large pharmaceutical enterprises have chosen the acquisitions of small enterprises (see figure 2, pg. 11) as an option for developing new technologies (Comanor and Scherer, 2013; Gleadle *et. al.,* 2013; Hopkins *et. al.,* 2013; Hopkins *et. al.,* 2012; Light and Lexchin, 2012; Higgins and Rodriguez, 2006; Munos, 2009; Paul *et. al.,* 2010).

Figure 1: Share of NME approved by large and small companies



Source: Munos, 2009, pg. 965

Figure 2: M&A in the pharmaceutical industry, in the USA and Europe, between 2006 and 2015



Fonte: Ernst & Young, Biotechnology Report: Beyond Borders, 2017, pg 80

The graphic above shows that M&A between pharmaceutical and biotech enterprises cannot be ignored in terms of deals and value.

As consequence the incorporation of competences outside the borders of the large pharmaceutical enterprises was done mainly though interactions with small enterprises. According to Sharp (1996), the large pharmaceutical enterprises, in a first moment, did not engage in creating biotechnology competencies, but they kept some research inside to develop some absorptive capabilities to keep up with the technical advance (Cohen and Levinthal, 1990). 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 and Katila, 2001; Cassiman and

Veuglers, 2007, 2006; Cullen and Dibner, 1993; Malerba and Orsenigo, 2015; Powell *et. al.,* 1996; Makri *et. al.*,2010; Gambardela, 1995; Hagedoorn *et. al.*,2002; Cloodt and Hagedoorn, 2006; Sharp, 1996).

The incorporation of small biotech companies into large pharmaceutical firms follow a model, in which research teams are maintained, and the small biotech firm productive capacity is dismantled. Each purchased company acts as a new R&D team, specialized in biotechnology, which was added to the set of innovation activities held by the large corporations (Schweizer, 2005). This integration model highlights the goal of pharmaceutical companies in incorporating biotechnology capabilities into their R&D through acquisitions.

The small enterprises ability to innovate is maintained through its incorporation as an R&D unit (Schweizer, 2005). Based on the interviews conducted by AUTHOR (2016) and on the model of integration showed by Schweizer (2005), it is possible to attest that acquisitions of small biotech enterprises are driven by the potentiality that small biotech enterprises can bring to the Big-Pharma's R&D. In that sense, several studies have pointed a positive relation between acquisitions of small enterprises and an increase in the acquiring technological output (Anderssen and Xiao, 2016; Ahuja and Katila, 2001; Desyllas, Hughes, 2007, 2010; Hussinger, 2010; Szücs, 2014).

In this article, we assume that acquisitions between large and small enterprises are driven by technological aspects. As an outcome, these acquisitions, indeed, increase the enterprise competence scope (Chakrabarti, *et. al.*, 1994, Desyllas; Hughes, 2007, 2010; Granstrand *et. al.*, 1992; Granstrand; Sjölander, 1990; Hussinger, 2010, Norbäck; Persson, 2013; Xiao, 2015). Acquisitions by themselves do not guarantee the incorporation of R&D competences within the acquiring enterprise. Other elements are necessary to fulfill this goal

1.3 Inventors role on small enterprises innovative output

This process of incorporating small enterprises, detailed by Schweizer (2005), may be considered successful, because these enterprises are distinguished in their R&D, specially, when these small enterprises span out from the academic universe.

Academic start-ups are underpinned in the research conducted by a group of scientists that enabled the firm creation (Colombo; Piva, 2012; Powell *et. al.*, 2005; Powell *et. al.,* 1996; Zucker; Darby, 1997, 2009). Therefore their research is the main element that drivers the acquisition.

Nevertheless, the process of successfully incorporating the competences outside the enterprises knowledge base, through the mere access of new technologies, is not an effective element for rendering new routines (Von Hippel, 1994, 1998; Powell and Snellman, 2004; Nelson and Winter, 1982). Much of the knowledge about a set of technologies and its mastery is held by its developers, making knowledge stick to its inventor (Brown and Duguid, 2001; Snell and Powell, 2004; Von Hippel, 1994, 1998).

As drug discovery activities become more complex and dependent on the knowledge and skills for its conduction (Amzel, 1998; Gassman *et. al.*, 2004; Macarron, *et al*., 2011; Pereira, Williams, 2007) the problems related to stickiness may increase (Brown and Duguid, 2001; Snell and Powell, 2004; Von Hippel, 1994, 1998). One way of attesting it is the outsource limit of R&D activities (Mowery and Rosenberg, 1989). In the pharmaceutical industry, as in other sectors, if R&D cannot be fully outsourced its core must be done inside the enterprise (Mowery and Rosenberg, 1989).

For instance, random screening technologies and computational models cannot build molecules by they own; they need a trained scientist able to recognize a possible molecule. Drug discovery is still highly dependent on the scientist skills, although, the industry has been facing a process of R&D industrialization (Nightingale, 2000; Nightingale and Madhi, 2006). Therefore, is not difficult to accept that inventors have a great effect on the enterprises technological outputs (Almeida *et. al.*, 2011; Grigoriu and Roathermel, 2014; Hess and Roathermel, 2011; Hohberger, 2016; Zucker and Darby, 1997, 2009; Zucker *et. al.*, 2006).

The new technologies incorporated by large enterprises, especially the ones dedicated to drug discovery and genetic sequencing, were born in universities. This fact even increase the importance of scientist role of developing and spreading these technologies outside the academic world and inside the economic environment (Colombo and Piva, 2012; Zucker and Darby, 1997; Zucker *et. al.*, 2006). The more innovative small enterprises have star scientists[2] as part of its workforce (Zucker *et. al.*, 2002). In addition, scientists do not work alone, their capacity to increase the enterprises innovative activity is also correlated to how they interact with other scientist within the same enterprise (Oettl, 2012; Grigoriu and Roathermel, 2014; Hess and Roathermel, 2011).

As scientist move from one to other enterprises they tend to keep researching their "own stuff" (Hohberger, 2016) this evidence a certain path dependence held by scientists over their research achievements.

[2]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.

In this process the same research line can be constructed in order enterprises if the main inventors are maintained.

Even though the knowledge held by scientists could be, arguably, of free access; much of the process that leads to the development and mastering of a new technology is extremely embedded in the scientist, or the group of scientists that developed the technology. Furthermore, the research of a scientist follows a path that do not depends on the place that he or she works (Hohberger, 2016). In conclusion, as large enterprises employ scientist they are attempting to master a specific technology by building inside research lines that started elsewhere.

2 Methodology

This study methodology starts by setting a comprehensive sample of large pharmaceutical enterprises. In order to do that three sources of data were used. The first source 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 (target), (ii) the acquiring companies (acquirer) and (iii) the amount spent. Based on this report the study can extract which companies were actively acquirers (have acquired more enterprises) and which ones spent more resources on M&A. The second source was the Forbes' list of the 2000 largest companies in the world[3] used as means of better selecting the larger enterprises. The Last source are the enterprises own annual reports that inform details about R&D and specific acquisitions.

These three sources of data were combined to set a comprehensive set of large enterprises relevant in terms of revenues, R&D and M&A expenditures. The HBM informs the relevancy of acquisitions and the Forbes indicates the relevant enterprises in terms of revenues. Finally, the annual reports inform the enterprises R&D expenses. Not all large enterprises are intensive acquirers and some less relevant enterprises may spent a great amount on M&A, but all large and relevant Big-Pharma have a similar R&D investment. Thus, the combination of Forbs index, the HBM report and the enterprises annual report enables choosing both large relevant enterprises and intensive acquirers.

We select among the 10 larger enterprises whose were the most active acquires acquirers. The final result and therefore the sample are: (i) Pfizer; (ii) Johnson & Johnson; (iii) Roche; (iv) Sanofi; (v) Astra-

[3] This study used the 2013 edition

Zeneca; (vi) Abbott-Laboratories; (vii) Glaxo SmithKline (GSK) and (viii) Merck. Therefore, the sample is composed by these 8 large enterprises that acquired 54 small enterprises.

Finally, the patent data was collected at the PatFT (Patent Full-Text and image database), a database from USPTO.

2.1 Sample relevancy

The sample relevancy can be attested in the following table.

Table 1: Sample Information (US$ Billions)

Companies	R&D (2012)	Total Expenses in M&A	Annual Average Expenses in M&A (2005-2012)	R&D/Revenue	Annual Average Expenses on M&A/Revenues	Annual Average Expenses on M&A/R&D
Pfizer	6,6	76,5	9,5	13%	18,6	1,4
Johnson &Johnson	5,3	4,5	0,5	21%	2%	0,09
Merck & Co	8,1	2,9	0,3	17%	1,10%	0,05
Roche	14,16	48,3	6	35%	14,60%	0,4
Astra Zeneca	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
World Total	135	585,48	73,18	-	-	0,54
Total (sample)/World Total	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' expenditures in R&D. In addition, these 8 enterprises account for the 32% of all expenditures in M&A in the pharmaceutical industry.

2.2 Use of Inventors as measure

As vastly discussed in the literature the use patents have significant problems (Griliches, 1979; Griliches *et al.,* 1986, Pakes and Griliches, 1980) that is greater when one thinks on a useful theory of knowledge (Mokyr, 2002). Nevertheless, patens are highly used and considered as proxies of technical knowledge (Ahuja, Katila, 2001; Andersson, Xiao, 2016; Cloodt, Hagedoorn, Van kranenburg, 2006; Desyllas; Hughes, 2007, 2010; Hagedoorn, Duysters, 2002; Xiao, 2015, among others).

Arguably, patents are inventions that partially represents the amount of knowledge available for the enterprises that engage in acquisitions. In essence, patents may be treated as techniques in accordance with Mokyr (1993, 2002) definition of the later. Nevertheless, each invention has behind it an inventor or a group of them. Therefore, inventors are the main element responsible producing new technology (Colombo, Piva, 2012; Hohberger, 2016; Hohberger, 2016; Almeida, Parada, 2015; Oettl, 2012; Zucker, Darby, 1997; Zucker *et. al.*, 2002). Even though the inventor is mentioned on each patent, the knowledge that them hold surpass the patent scope, making them a good source of embedded knowledge.

The statement above holds tighter in small enterprises with few employees and patents (Author, 2016). Thus, the people identified as inventors represent a major part of knowledge incorporated among enterprises.

In this line of thought an enterprise that needs to master a technology developed by the small enterprise, must employ the inventors responsible for producing the same technology. Arguably, the evolution of technology and the successful incorporation of inventors lead to new patents. Therefore, every time an inventor develop a patent for the large enterprise he is producing knowledge and technology that will be eventually used by this same large enterprise.

This incorporation, traceable through patents, is expressed in a 'movement' of inventors that move from the target to the acquirer enterprise. In order to track this movement we analyzed individually all the 2.803[4] patents issued by these 54 small enterprises. The study got a total of 1.971 inventors. At the USPTO we search each of the inventors to compile who had developed a patent assigned by the large acquiring enterprise after it acquired a small enterprise. In other words we look for inventors that started to employ their embed knowledge for the large enterprise.

By tracking the inventor's movement this article could observe the inventors that were incorporated by the large acquiring enterprise. The mathematical relation between the inventors in the small enterprises and the ones that move to the large enterprises is the "inventors usage" that is presented as a simple percentage index.

2.3 Research trajectory incorporation

The research trajectory incorporation is an adaptation based on Hohberger (2016). In essence, Hohberger (2016) tries to identify if star scientist are able to developed innovations on their past research and if other scientist can create inventions based on others star scientist past research. Our idea, in this article, is focused on the inventor that move from the small to the large enterprise and has referenced his past work, enabling the continuation of his research trajectory on the large enterprise.

[4] The number of patents is the informed in a search for assignee name in the USPTO.

With this in mind, the research trajectory incorporation is a method, developed in this article, that follows some steps. The first step is given by the inventor's usage, which give us the enterprises that had incorporated inventors. As showed before, from the 54 small enterprises, 31 had at least one of its inventors incorporated by the large enterprise. The second step consist on compiling all patents issued by the inventors of these 33 enterprises, in the period they were employed by the small enterprise. The third step encompass looking for these inventors' patents that reference their own past work. Summing up, we are looking for patents assigned by large enterprises that reference patents assigned by small enterprises, but both must be developed by the same inventor.

For example: the inventor A developed 3 patents for the small enterprise Y that was later acquired by large enterprise X. In the acquisition process, inventor A was incorporated by X. In the large enterprise, A has issued 3 patents and among these 3 patents he has referenced 2 patents that he developed when he had worked for the small enterprise Y. In the end, what is seen is that the large enterprise is not only incorporating the inventor's knowledge but his research, now, is been conducted in acquirer enterprise, therefore we are seeing a process of research incorporation.

Clearly we use the acquisition phenomenon as the main event. Therefore we can think on processes after the acquisition and before the acquisition. For that and to make the comprehension of the next tables clear we chose to adopt the following nomination:

Prior patents: refers to patents developed by the incorporated inventor and assigned by the small enterprise

Following patents: the patents developed by incorporated inventors and assigned by the large enterprise

Referenced Patents: patents used as reference in the following patents. In our case, all referenced patents are prior patents but not all prior patents are referenced patents

Generated Patents: patents that have as reference at least one prior patent. In our case all following patents are generated patents, but not all following patents are generated patents

The research trajectory incorporation evidences a full incorporation of knowledge. As inventors continue their work they are also internalizing and spreading their knowledge across the acquirer enterprise.

3 Results and Discussion

The incorporation of inventors is a first step in order to evidence the relevance of embedded knowledge in the large enterprise strategies. Acquisitions by themselves may have several meanings and they do not show commitment of the acquirer enterprise to its target technical development. One possible way of realizing the commitment is through patent citations, because the more relevant patents are the more cited ones (Hall; Jaffe; Trajtenberg, 2001, 2013) and patent citation increase the enterprise's market value (Hall *et al*., 2005).

Other possible way is through the incorporation of inventors, when key people are maintained, the big-pharma is looking to internalize critical elements in the other enterprises' innovative capabilities (Author, 2016). Furthermore, by bringing the relevant inventors, the large enterprises are trying to emulate inside its borders the interaction among inventors in the small enterprises dynamics. These two elements are essential for the innovative output (GRIGORIOU; ROTHAERMEL, 2014; OETTL, 2012; SCHWEIZER, 2005)

We propose that the idea of "inventors usage" allows observing the incorporation of inventors, therefore, commitment. As shown in the table below, the incorporation of new inventors is a common strategy.

Table 2: Inventor's usage

Small acquired enterprises	Total of inventors in the acquired companies (A)	Inventors that started to patent for the large enterprise (B)	Use of Inventors (B/A)
Roche	95	48	**51%**
Abbott-Laboratories	44	19	**43%**
Sanofi	137	42	**31%**
Pfizer	329	49	**15%**
Merck	255	32	**13%**
GSK	680	58	**9%**
Astra Zeneca	275	20	**7%**
J&J	156	9	**6%**
Total	1971	277	**14%**

Source: own elaboration

The average inventors use is 22%. In table 2 the 8 large pharmaceutical companies have, in different degrees, incorporated the inventors from the acquired firms. Some enterprises as Abbott-Laboratories and Roche have used a large share of inventors; while J&J, Astra-Zeneca, and GSK just a few. Although the incorporation of |inventors is disseminated among the sample, the degrees of incorporation are heterogeneous. This fact is even clear when one looks at the small enterprises individually, as shown in the following tables.

Table 3: Roche use of inventors

Small acquired enterprises	Total of inventors in the acquired companies (A)	Inventors that started to patent by Roche (B)	Use of Inventors (B/A)
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%

Source: own elaboration

Table 4: Abbott-Laboratories use of inventors

Small acquired enterprises	Total of inventors in the acquired companies (A)	Inventors that started to patent by Abbott-Laboratories (B)	Use of Inventors (B/A)
Facet-Biotech	30	18	60%
KOS-Pharmaceuthicals	14	1	7%

Source: own elaboration

Table 5: Sanofi use of inventors

Small acquired enterprises	Total of inventors in the acquired companies (A)	Inventors that started to patent by Sanofi (B)	Use of Inventors (B/A)
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%

Source: own elaboration

Table 6: Pfizer use of inventors

Small acquired enterprises	Total of inventors in the acquired companies (A)	Inventors that started to patent by Pfizer (B)	Use of Inventors (B/A)
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%

Source: own elaboration

Table 7: Merck use of inventors

Small acquired enterprises	Total of inventors in the acquired companies (A)	Inventors that started to patent by Merck (B)	Use of Inventors (B/A)
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%

Source: own elaboration

Table 8: GSK use of inventors

Small acquired enterprises	Total of inventors in the acquired companies (A)	Inventors that started to patent by GSK (B)	Use of Inventors (B/A)
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

Table 9: Astra-Zeneca use of inventors

Small acquired enterprises	Total of inventors in the acquired companies (A)	Inventors that started to patent by Astra-Zeneca (B)	Use of Inventors (B/A)
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%

Source: own elaboration

Table 10: J&J use of inventors

Small acquired enterprises	Total of inventoris in the acquired companies (A)	Inventors that started to patent by Pfizer (B)	Use of Inventors (B/A)
TransForm Pharmaceuticals	33	8	24%
Crucell	81	1	1%
Omrix	22	0	0%
Respivert	15	0	0%
Corimmun	5	0	0%

Source: own elaboration

The incorporation of inventors varies very much among enterprises. For instance, GSK has just used 9% of the small enterprises inventors, but it has incorporates inventors from almost all (with the exception of one) the small enterprises it acquired. On the other hand, Roche has used a high degree of inventors but it has incorporated inventors from half of the acquired companies.

Individually some small enterprises can be highlighted. There are substantial cases of inventors incorporation such as: Vax Design, Piramed, Reliant Pharmaceuticals, Rinat Neuroscience and others. The individual cases show a pattern among the Big-Pharma, there is always, at least, the incorporation of inventors from one enterprises.

The number of inventors incorporated is not high, as mentioned before, just in few cases 100% of the inventors were internalized. In essence, the cases of inventors incorporation is aligned with Blomkvist; Kappen; Zander (2014) perception of technical advances that is been put forward by a small group of people. Thus the few incorporated inventors may generate great impact on technology development.

That fact also justify the literature attention on star scientists, being them just a few that are responsible for a great amount of knowledge production (Grigoriou; Rothaermel, 2014; Hohberger, 2016; Oettl, 2012; Zucker; Darby, 2009). Therefore, when the Big-Pharma incorporate inventors the company is attempting to enjoy these star-scientist effect.

Based on the literature the incorporation of inventors have important outcomes for the large enterprise. According to Hohberger (2016), by incorporating inventors, the large enterprises are internalizing the research paths i. e. the Big-Pharma is bringing inside its borders the knowledge that was developed outside. We can look in closer detail to the incorporation of inventors in order to observe the incorporation of research trajectories.

The next table enables comparing the enterprises acquired, the enterprises that had at least one inventor incorporated and the enterprises that had at least one of its inventors' research trajectory internalized.

Table 11: Comparison between enterprises acquired with inventors incorporation and research trajectory incorporation

Enterprises	Number of enterprises acquired	Acquired enterprises with incorporated inventors	Acquired enterprises with research trajectories internalized
Pfizer	11	5	2
J&J	5	2	0
Merck	7	4	4
Roche	6	3	3
Astra-Zeneca	7	3	1
Sanofi	6	3	1
GSK	10	7	3
Abbott-Laboratories	2	2	0

Source: own elaboration

Table one can be understood as process that starts in the acquisition (column 2) and ends in the inventors research trajectory internalization. Clearly that are too few research trajectories internalized.

We can also analyze in terms of inventors and their products (patents) as show in the next table

Table 12: Internalized Research Trajectories and Patents Relevancy

Enterprises	Inventors Incorporated	Inventors with research trajectories Internalized	Prior Patents	Referenced Patents	Generated Patents
Pfizer	49	9	115	32	8
J&J	9	0	21	0	0
Merck	32	18	257	34	33
Roche	48	37	81	37	33
Astra-Zeneca	20	1	43	1	1
Sanofi	42	7	10	5	2
GSK	58	19	345	20	12
Abbott-Laboratories	19	0	0	0	0

Source: Own elaboration

This table points to the importance of a small group of inventors that had their research internalized. Not only their single inventions were relevant but based on their past work new inventions were created, somehow building a research trajectory in the enterprise. This research stated outside the large enterprise borders but as the Big-Pharma acquired and maintain some relevant inventors the Big-Pharma was able internalize some research done outside its borders and apparently successful incorporated it in tis R&D

The incorporation of inventors is not only a way of mastering the developed technology, but is a strategy to appropriate the outcomes of the research conducted by the inventors. Many small enterprises have no patents, but the research conducted by their R&D team is enough to draw the attention of a Big-Pharma (AUTHOR, 2016). This fact can be seen as a cycle where the technology draw the attention of the large enterprise, after its acquisitions, this same technology can evolve as the inventor keep researching related subjects.

Conclusion

This study departed from the increasing complexity in the pharmaceutical R&D. The industry has developed two trajectories, being one: the further advance of chemistry related competences and the other: based on the diffusion of biotechnologies though a molecular biology trajectory. This process made R&D a multidisciplinary activity where competences outside the large pharmaceutical enterprises borders are essential. The pharmaceutical R&D competences are impossible to be dominated by one enterprise alone. In order to cope with that the Big-Pharma had to seek for these competences outside its borders.

Molecular biology was created at universities, the agents capable of transforming these field of knowledge into techniques also were from the academic realm. As a characteristics the enterprises that held the competences needed form the large enterprises are outcomes of academic research. Furthermore, small enterprises became relevant agents in the share of innovative output in the pharmaceutical industry. Nowadays, these firms are as innovative as the Big-Pharma. Therefore, the competitiveness in the large pharmaceutical companies depends on the access of these enterprises to the knowledge developed by the small innovative ones.

Among the many strategies for the Big-Pharma, the acquisitions were chosen in this article, mainly, because it has grown intensively over the years, specially, when it involves large and small enterprises. Acquisitions are a first step into mastering new competences but this process depends on how the large enterprise deals with the elements that generate knowledge in the small enterprise, in other words, the large enterprises have to incorporate the knowledge producers in the small enterprises.

The knowledge producers are the ones responsible for producing new technologies, in this study, the inventors were considered. Therefore, the incorporation of inventors by the large pharmaceutical company is essential for mastering and creating new competences. The Big-pharma have to incorporate these inventors and allow them to produce in order to incorporate new competences in its routines.

The inventors usage, proves that Big-Pharma are extensively incorporating the knowledge producer from the target companies. As inventors are being incorporate the Big-Pharm are internalizing important knowledge and also building new research lines internally.

As advances of these article we point to the literature gap it fills. The focus on a single element of knowledge incorporation allows to understand in a better way the Big-Pharma strategy towards small enterprises. In addition this study contributes by proposing a really detailed methodology for identifying knowledge incorporation, being the inventors use and the research strategy incorporation

This study has dealt with an enormous amount of data, but the analyses was simple. Nevertheless, this article has explored a new element in the acquisition studies. While the majority of studies are dealing with post-acquisition performance or pre-acquisition drivers, there are only few studies dealing with the process in between pre-acquisition and post-acquisition. In the end, is this period that defines the success or failure of an acquisition.

This article left some questions unexplored. First it will important to correlate the inventors that were acquired and the technology developed by them, in order to observe if the incorporation of inventors is linked to some specific characteristic in the technology developed, like: novelty, importance, technology field. Another important element to further developed is to identify why some inventors produce more patents for the large enterprise while others no.

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