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Evolution of Capabilities in the Discovery Cycle of an Innovation in the Pharmaceutical Market

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ABSTRACT

The objective of this study is to analyze the evolution of dynamic capabilities in the discovery cycle of an innovation in the pharmaceutical market of erectile dysfunction in the period of 20 years. To achieve this, two distinct and complementary concepts were applied: Models of March (1991) to exploitative and explorative discovery in the organizational learning process and the three components of dynamic capabilities. The result showed that the components of the capabilities may be identified in the discovery cycle of Viagra®. The study confirms the existence of a stock of knowledge among the companies in the pharmaceutical market of erectile dysfunction as well as a large absorptive capacity among all of them.

Keywords: Marketing, Innovation, Pharmaceutical Industry, Property Intellectual
JEL Classifications: M1, M3, M19

1. INTRODUCTION

Portfolio management and intellectual property rights are central to pharmaceutical organizations (Veiga et al., 2013) where the process of research and development (R and D) is critical to the success of innovative products. This sector is embedded in a rapidly changing environment, characterized as hypercompetitive (Wang, 1997; Biedenbach and Muller, 2012). Under conditions of high global competition and rapid technological advances, it is not enough companies engage in excellence performance or in technical efficiency. The competition in the pharmaceutical market encompasses the ability to develop systematic process by means of production and application knowledge, because innovation involves building and expanding organizational capabilities over time.

The development of new pharmaceuticals products is one of the mechanisms by which companies create, integrate, recombine and share resources, i.e. there is a dynamic and reciprocal relationship between the efforts of product innovation and the use and development of the capabilities of a company (Danneels, 2002). Once theory of "dynamic capabilities" (Teece et al., 1997) attracted attention to the need for renewal of the company's capabilities in changing environments, research began to focus on the dynamic nature of capabilities and how these develop along the cycle of discovery of a new product (Danneels, 2002).

Thus, this study aims to investigate the evolution of capabilities in the discovery cycle of an innovation within the pharmaceutical market in the medicine segment for erectile dysfunction. For this, two distinct and complementary concepts will be applied: Models of March (1991) for exploratory discovery (exploitative) and for investigative discovery (explorative) in the organizational learning process and the three components of dynamic capabilities named absorptive capacities, innovativeness and adaptability (Biedenbach and Muller, 2012).

The study of erectile dysfunction market allows investigating the evolution of capabilities in the discovery of an innovation at all stages of the technological trajectory of a market, the launch of a radical innovation to the release of generic versions of the product. Besides this practical importance, the pharmaceutical

market is large with high sales volume and constancy, which can accommodate several incremental innovations. Erectile dysfunction is a chronic disease in which large numbers of people treat themselves for years and new patients are added every day. It is an important object of study that is able to provide information not fully catchable by other objects of research.

This study highlights the internal and external arrangements of R and D of pharmaceutical companies, which can be defined as an evolution of its capacity limits. Internally, companies can leverage their resources and stocks of knowledge to achieve innovation, but these organizations may also seek external knowledge and heterogeneous resources and can identify and capitalize on opportunities in emerging markets has never worked before. Based on these premises, this paper approaches three research questions: (i) Through the patent data, it is possible to evaluate the discovery cycle of inhibitors phosphodiesterase Type-5 (PDE-5)[1] and correlate the adaptive, absorptive and innovative capabilities? (ii) What are the major companies that have demonstrated adaptive capability to identify and capitalize opportunities on market erectile dysfunction? (iii) What are the major companies that have demonstrated absorptive capability to benefit from a stock of knowledge in the erectile dysfunction market?

This research contributes to neglected areas within the field of research on dynamic capabilities by exploring how the discovery cycle of a pharmaceutical product is affected by the loosely articulated networks established among various pharmaceutical companies. Furthermore, the research uses patent data, an unusual source of research on dynamic capabilities, and an object of specific research and unexplored in the light of this theory. More broadly, the results of this study provides tangible explanations of adaptive, absorption and innovation capacities, differentiated pharmaceutical companies in turbulent and uncertain environment of the erectile dysfunction market. This work is divided into four parts, beyond this brief introduction. The following describes the theoretical framework, research methodology and analysis results. The final part includes consideration of the findings of each research question.

2. THEORITICAL BACKGROUNG

2.1. Dynamic Capabilities in Pharmaceutical Industry

The use of the term strategic capabilities has its origin in the resource-based-view (RBV) of a firm. The RBV states that an organization develops based on its collection of resources and their use (Penrose, 1959). Other researches added to RBV the concept of capabilities (Richardson, 1972) or matching individual skills with organizational capabilities (Nelson and Winter, 1992). The dynamic capabilities are a special type of organizational ability with special relevance for gaining competitive advantage in terms of volatility and turbulence of the organizational environment (Teece et al., 1997). Although the concept of dynamic capabilities have been extended and refined by several researchers (Eisenhart and Martin, 2000; Zollo and Winter, 2002; Helfat et al., 2007; Teece, 2007), the roots of the original concept remains, i.e., dynamic capabilities allow organizations to integrate, build and reconfigure their resources and skills and help maintain performance in the face of rapid changes in the business environment.

In this concept, the dynamic capabilities represent strategic processes whose objective is shaping the functional skills (Pavlou and Sawy, 2006), thus involving the perception of the environment (adaptive capability), knowledge generation (innovativeness), coordination of activities and integration of resources (absorptive capability). Value creation comes by identifying new opportunities and organizing its internal, managerial and technological processes effectively (Teece et al., 1997), restructuring of internal and external competencies to achieve competitive advantage (Teece, 2007).

The concept of dynamic capability fits perfectly to the process of pharmaceutical R and D, which is an uncertain business, multifaceted, highly complex and it requires a strong interaction of sources of several origins. In the pharmaceutical industry, companies recognize that the available technologies and the pieces of knowledge can originate from internal and external organizational boundaries (Santos, 2003; Bianchi et al., 2010). Thus, external actors can influence the company's investment in internal R and D, expanding the opportunities of combining knowledge and unconnected previously capabilities (Dahlander and Gann, 2010).

To survive in an environment characterized by rapid change, companies need to continually adapt their knowledge and skills. When analyzing the pharmaceutical industry must think about approaches that consider a dynamic market with limited time span and alternation of creation cycles and value destruction (Schumpeter, 1992) in the field of resources and capabilities no longer guarantees lasting competitive advantages (Danneels, 2002; Higa, 2011). In a world where innovations are quickly duplicated, patenting is a relatively effective response to the vulnerability inherent in the product information. The patent does not guarantee total protection because innovation in itself reveals information which, moreover, could be protected by secrecy. The information made public by the patent allow "inventing around" (Winter, 1998) or "invention patents" (Lichtenberg and Philipson, 2011) where the emphasis is not given to the capacity of knowledge production (exploration) and rather the ability to adopt knowledge (exploitation) produced by other companies (Gilsing and Nooteboom, 2006).

The following subsections detail these distinct and complementary concepts: The three components of dynamic capabilities named absorptive, innovation and adaptability capacities (Biedenbach and Muller, 2012), as well as the model of March (1991) for exploratory discovery (exploitative) and for investigative discovery (explorative) during the evolution of pharmaceutical dynamic capabilities.

2.2. Absorptive Capability

Absorptive capability is the ability of a firm to recognize the value of new external information, as well as to absorb them and apply them to a commercial purpose (Cohen and Levinthal, 1990). Studies

1 Inhibitors of PDE-5: Pharmaceutical class which belongs Viagra®

on absorption capacities include research on R and D (Harhoff and Reitzig, 2004), knowledge management (Corso et al., 2006; Lagerström and Anderson, 2003), organizational structures (Caloghirou et al., 2004; Lenox and King, 2004; Van den Bosch et al., 1999), inter-organizational relationships (Lane and Lubatkin, 1998; Caloghirou et al., 2004; Fernández et al., 2012) and integration with customers (Johnsen and Ford, 2006).

The absorption capability occurs when knowledge from the company outside is evaluated and then integrated through imitation, licensing, acquisition or interorganizational collaboration. Generally, the external knowledge absorption occurs through gathering of experts, conversation between employees from rival companies, hiring employees from competitors, by reverse engineering of products and by analyzing scientific articles and patent databases (Carolis, 2003; Biedenbach and Muller, 2012). Such capability makes people more aware and sensitive to changes in the business environment knowledge, allowing the identification and assessment of the implications of technological change. Furthermore, it enables the development of a broader knowledge base, which may become a source of competitive advantage (Santos, 2003).

Firms with higher absorptive capacity demonstrate greater capacity for learning and integration of external information, as well as greater ability to transform this information into know-how for the corporation (Wang and Ahmed, 2007). Moreover, firms with absorptive capability (Wang and Ahmed, 2007): (i) Demonstrating commitment to the long-term resources in the face of uncertainty, (ii) seeking to develop new technologies for internal and external learning, the latter through various stakeholders, (iii) analyzing carefully the development of new technologies for training and share information within multidisciplinary teams, (iv) developing and utilizing complementary technologies and, (v) having a high level of knowledge and skills in areas relevant to the application of new technology.

The ability of a company to acquire new technologies and absorb them into existing internal knowledge is an important factor of dynamic capabilities in various industries (George, 2005; Salvato, 2003; Verona and Ravasi, 2003), primarily for the pharmaceutical industry. Firms with absorptive capability prioritize the departments of R and D as a stimulus to acquire, assimilate, transform and exploit knowledge (Zahra and George, 2002) and thus absorb new technologies and organizational skills. For firms with absorptive capability, internal R and D have two main functions (Cohen and Levinthal, 1990; Oltra and Flor, 2003): (i) The creation and integration of new knowledge, which emphasizes the cumulative nature of knowledge, and (ii) the ability to apply knowledge, which is dependent on the historical path. These companies have the advantage that their results are more easily appropriated, once they are specific to the company, and intellectual property can be legally defended. As a disadvantage, just rely on the absorption of knowledge can block the company and limit it to specific paths of technological development (Santos, 2003).

2.3. Innovation Capability

The term innovation can be defined as the development and use of new ideas or behaviors in the organization (Wang and Ahmed, 2004; Damanpour and Wischnevsky, 2006). A new idea could be a new product, service or method of production (technical innovation) or a new market, new organizational structure and new administrative system (administrative or organizational innovation). Additionally, as indicated by the own definition, the innovation capability includes several dimensions and depends on the introduction of new scientific knowledge that make possible the understanding of previously incomprehensible phenomena.

The more innovative a company is, the greater its dynamic capabilities (Wang and Ahmed, 2007). The emergence of technological trajectory is triggered by technological paradigm or the discontinuity, which is often related to scientific discoveries. In some industries, such as pharmaceuticals, for example, the emergence of technological trajectory switches revolutionary and evolutionary periods, allowing the emergence of a large number of incremental innovations followed some discontinuous innovations (Sternitzke, 2010; Özer, 2012).

The primary purpose of technological innovation is to introduce a change in the organization to create new opportunities or to explore existing ones (Carolis, 2003). Pharmaceutical organizations, in turn, operate under high global competition, rapid technological advances and resource scarcity, which makes innovation an essential factor for growth, efficiency, and last resort for the very survival of organization that competes on technological bases (Damanpour and Wischnevsky, 2006).

The most traditional classification characterizes innovation as radical or incremental (Schoenmakers and Duysters, 2010; Biedenbach and Muller, 2012). Incremental innovations consist of smaller improvements or modest adjustments to existing products or technologies. The individual impact of this type of innovation is usually limited. The radical innovations, on the other hand, are generally considered to be a dangerous rupture of existing practices. Radical innovations exhibit key features that are inherently different from existing products or technologies. In general, in an incremental innovation dominates the current knowledge and innovation there is a radical transformation of the prevailing knowledge (Subramaniam and Youndt, 2005).

For radical innovations there is little accumulated information on the pharmacological aspects of the action of a new drug mechanism, as well as the administrative aspects in relation to marketing of the new medicine. The lack of information for management decision making is accompanied by a high degree of uncertainty. For this reason, in addition to the capabilities of the firm and the individual efforts, radical innovations depend on the social capital of the company and the possibilities of this social capital provide a social epistemology that can support the development process (Baba and Walsh, 2010). The corporate social capital is the key to overcoming the inherent uncertainty of the radical innovation process.

2.4. Adaptive Capability

Adaptive capability is defined as the ability of a company to identify and capitalize on opportunities in emerging markets (Chakravarthy, 1982; Hooley et al., 1992; Miles and Snow, 1978). The adaptive

capability focuses on searching for efficiency and exploring strategies (Staber and Sydow, 2002). The key element of adaptive capability is the ability to respond to external market-product opportunities (Chakravarthy, 1982), which can trigger an increase organization performance (Bourgeois, 1980; Snow and Hrebiniak, 1980).

Companies that have high levels of adaptive capability exhibit dynamic capabilities (Teece et al., 1997) and show ability to align internal resources with external demand (Alvarez and Merino, 2003; Camuffo and Volpato, 1996; Forrant and Flynn, 1999), determinants factors for the evolution of organizational structures (Wang and Ahmed, 2007) and survival of the company against environmental changes. These companies respond to external opportunities, explore the market, manage customers and consumers, allocate resources to market activities and respond to changes more quickly and effectively (Oktemgil and Gordon, 1997). In this sense, some authors consider the adaptive capability as a form of business intelligence, which includes verifying pipeline of R and D competitors and analyzing possibility of incremental innovations in scalable and profitable markets (Biedenbach and Muller, 2012).

The pharmaceutical industry exhibits exceptional flexibility and adaptability within a competitive environment of intense changing (Achilladelis and Antonakis, 2001). The generation to generation transition requires considerable adaptive capability on the individual pharmaceutical company's side. These companies were forced to drastic structural changes, such as leaving their products, technologies, and traditional markets to develop new ways to adapt to new competitive processes. Companies that failed in these settings were acquired or merged with more successful competitors.

In general, the pharmaceutical industry tries to avoid the "inertia of activity," which is the company's trend to persist in a single technological trajectory trapped in ways of thinking and working that brought success initially. The only use of internal knowledge and maintenance of corporate technological tradition may represent a superior strategy for pharmaceutical companies, but when the environment changes, the company may not be able to adapt and survive (Carolis, 2003). However, only coordinating competencies and combining knowledge beyond corporate boundaries may not be enough, organizations need to interact with other companies, which makes the adaptive capability is directly related to absorptive capability (Biedenbach and Muller, 2012).

In short, the adaptive capability aligns internal organizational factors with external environmental ones. The absorptive capacities emphasizes the importance of acquiring external know-how, and combine them with internal knowledge, as well as taking necessary knowledge absorption for the organization to use them. The innovative capability, in turn, contributes in terms of new products and/or markets. These three components of dynamic capabilities are present in the discovery of a new medicine cycle, as detailed in the next subsection.

2.5. Discovery Cycle of a Product and Dynamic Capability

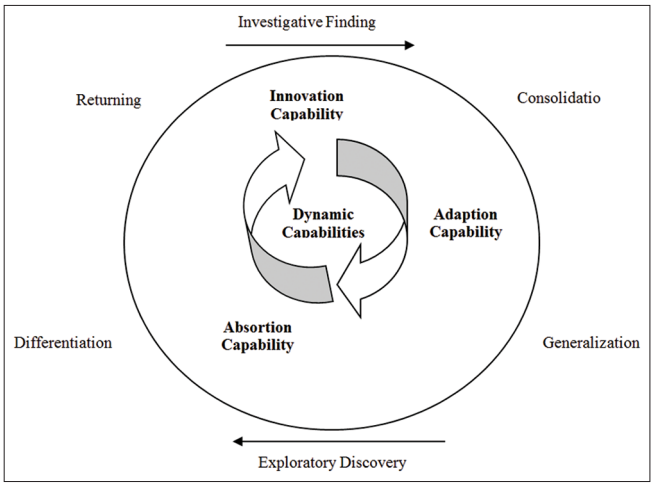
The pharmaceutical industry is dedicated to the development and commercialization of therapeutic medicines and it is the industry most intensively linked to the processes of R and D in almost all countries (Veiga et al., 2014). Launching a new product on the market is a hard work and time consuming. The discovery process is complex and it takes risks of a variety of laws and regulations in relation to patents (Veiga et al., 2013), the experimental evidence and marketing of medicines. Pharmaceutical data show that the development of a new medicine takes approximately 11.5 years and consuming 800 million (Sternitzke, 2010). Furthermore, only one in 5000 of medicine gets to the market and one in a thousand survives clinical trials.

In general, it could be said that recent developments in strategic research and heuristic R and D in the pharmaceutical industry can be characterized by two main regimes coexist: The first regime is based on assumptions and biological molecules that tend to be specific to data fields of application, the second regime is characterized by the emergence of new generic tools in the form of cross-technology (Orsenigo et al., 2001). In both cases, the pharmaceutical industry provides an intense process of R and D for cumulative learning and the absorption capabilities, innovation and adaptation obtained by interaction with other companies and market experience (Bianchi et al., 2010; Dahlander and Gann, 2010).

For a new medicine product, exploratory discovery (exploitative) and investigative finding (explorative) are mutually related factors and built upon one another, as illustrated in Figure 1 (Gilsing and Nooteboom, 2006). The term "exploratory discovery" refers to the efficient use of assets and capabilities available to ensure survival in the short term. The term "investigative discovery" refers to employment of new capabilities needed for long-term survival. For the company to remain in a specific market, it must continually combine investigative and exploratory discoveries, building a stage on the other.

The exploratory discovery begins when a variety of content (concepts, technologies, products or practices) emerges from the investigative discovery. As a result of the reduced uncertainty in the consolidation phase, the demand increases and new companies are interested in the sector. The new combination of technology/

Figure 1: Discovery cycle of a product



Source: Adapted of Gilsing and Nooteboom, 2006

product/market develops into a dominant design and knowledge becomes codified, which enables a faster and greater risk of overlapping diffusion. As a result, the variety decreases and the focus is changed to the learning process "single loop" between the companies.

The generalization phase starts with the opening of new varieties of application contents, which can be ordered in a voluntary activity expansion. In economic terms, there is some pressure to extend the market from stagnating original context. While some firms may actively search for new application models, some models can be imposed by external niches through new market conditions and technology. In this context, the generalization creates the necessary basis for the initial of investigative discovery.

To maintain the exploratory phase detection, there is an attempt to make only small adjustments to established practices, which is called phase of differentiation. The insights into the differentiation can come from prior experience or knowledge accumulated. The key factor is that these insights easily fit in practical experiences, which determines an incremental innovation, limited complexity, and without modifying the structure of existing network. However, when differentiation is not enough or the new context indicates new opportunities, deeper changes are needed, which characterizes the phase of retribution.

At the stage of returning, considering that the family practices failed, the experiments are conducted with new elements from new contexts. If new elements perform better, they are incorporated in the established capabilities. Experimentation with new elements allows testing new potential while questioning the existing basic principles. In other words, the stage of returning is the fundamental point between exploratory and investigative discovery. On the one hand, returning allows the permanence of continuous operation, while on the other hand provides insights into the potential of new elements and the constraints imposed by the existing design for the realization of this potential.

Once the hybrid practices begin to emerge, the returns and inconsistencies are reduced, the complexity increases and provides incentives and insights for a more radical architectural change. This new structure of old and new elements represent the investigative phase of discovery of new combinations. This phase shows a radical reconfiguration of the old system since the exploratory phase detection is not consistent with the emerging new.

Figure 1 illustrates the process of innovation within the principles of evolutionary thinking and demonstrates how absorptive, innovative and adaptive capabilities fit into the discovery of a new pharmaceutical product cycle. The consolidation and generalization, companies with adaptive capabilities identify and capitalize on opportunities in emerging markets. In the exploratory phase of discovery through the absorptive capability, incoming companies perform minor adjustments to established practices and generate differentiation with formation of incremental innovations. However, when deeper changes are needed, begins the stage of returning where the innovation capabilities represent fundamental skills to the organization. All these concepts are introduced through the pharmaceutical market of erectile dysfunction, the research object of this study.

3. METHODOLOGY

The following subsections describe the rational and systematic procedure designed to provide answers to the research questions. It will initially described the research object, the pharmaceutical market of medicines for erectile dysfunction, then the survey data represented by the database Derwent Innovations Index® patents (http://thomsonreuters.com/derwent-innovations-index/) and, finally, the theoretical model of each research question.

3.1. Study Object: The Erectile Dysfunction Market

In recent decades, health professionals have lived two of their biggest challenges towards sexuality: "Risk prevention of sexually transmitted diseases and pregnancy, as well as the acquisition and/or maintenance of the quality of male and female sexual performance" (Abdo and Afif-Abdo, 2010. p. 11). Both men and women are subject to the difficulties that the World Health Organization called sexual dysfunctions. The most common sexual dysfunction in men after age 40 is erectile dysfunction, defined as the persistent or recurrent inability to attain and/or maintain an erection adequate for completion of the sexual activity (Lue et al., 2004). Worldwide, the prevalence of erectile dysfunction should increase from 152 million men in 1995 to 322 million by 2025 (Ayta et al., 1999).

How erectile dysfunction can be devastating for male pride, it is not surprising that over the centuries many treatments have been proposed for the problem. The most common treatment until 1998 was the therapy of penis self-injection. Spite of the evolution of treatments that this market segment achieved until 1998, many men at that time still chose to live with the problem instead of using vacuum pumps, self-injections or tablets (Katzenstein, 1998; Fazio and Brock, 2004).

They were efficacy, safety and convenience of oral administration that made sildenafil medicine (Viagra®) a vehicle of socio-cultural change (Morales et al., 2011). The discovery of PDE-5, which belongs to the class as Viagra®, resulted to the society experience a major transformation in cultural ways of conceiving male sexuality. The launch of Viagra® not only represented a radical innovation, but the creation of a new pharmaceutical market, a fact that enables an important object of study.

3.2. Research Data: Patents of Database Derwent Innovations Index®

This study is a descriptive, documentary, longitudinal cross-sectional survey. The research problem was addressed quantitatively and qualitatively justified by the nature of the object of study as well as the procedure used for data collection. As primary analysis, this study used data from the patent database Derwent Innovations Index®. The selection of data was performed by use of specific therapeutic classification of chemical compounds for products for erectile dysfunction, A61P-015/10. Patents were selected from January 1990 until December 2010, which involved pre-and post-discovery of the first PDE-5 inhibitor.

The use of patent data in research represents a unique opportunity for a conceptual or qualitative analysis of technological change. In general, information about patent allows company-level analysis, analysis of wide geographical and temporal distribution of innovations, study of overlays, creating indicators and analysis of the technological and economic trajectory of inventions (Grilich, 1990; Meyer, 2000; Choi and Park, 2009; Mendes et al., 2013). These statistics if approached with a view to establish a dialogue with other data, can provide information not catchable by other sources.

3.3. Theoretical Model and Research Questions

To assess the evolution of dynamic capabilities in the pharmaceutical market of erectile dysfunction in the period from 1991 to 2010 and at the same time, make inferences about the cycle of discovery of PDE-5, this study examined three research questions:

Question 1: Through the patent data, it is possible to evaluate the discovery cycle of PDE-5 and correlate adaptive, absorptive and innovative capabilities?

It is increasingly difficult for pharmaceutical companies to develop innovation capabilities and meet entirely innovative medicines (Angell, 2008; Glass and Poli, 2009). When analyzing the pharmaceutical industry must think about approaches that consider a dynamic market with limited time span and cycles of creation and destruction of value alternation in the field of resources and capabilities no longer guarantees lasting competitive advantages (Glass and Poli, 2009; Higa, 2011). Moreover, whenever a group of technological trajectory is formed within a particular industry, it dominates its commercial and technological development (Achilladelis and Antonakis, 2001) so that several companies identify and capitalize on new opportunities in this emerging market. In this sense, adaptive capability and absorptive capability of the pharmaceutical companies contribute to that research be conducted in specific areas with possible pharmacological discoveries "easier" and with lower costs (Carolis, 2003; Baba and Walsh, 2010).

Question 2: What are the major companies that have demonstrated adaptive capability to identify and capitalize on opportunities in the erectile dysfunction market?

Today, the research addresses the growing fragmentation of the innovation process so companies need to resort to internal and external competences to the inventive effort. Only an integrated management of the innovation process can ensure the success and maintaining the competitiveness of the organization. Accordingly, monitoring the competitive environment plays a key role, as it enables the network from internal and external corporate information on the market performance. It is the ability of the pharmaceutical company manages these tools to determine their effectiveness in managing their innovations and evaluating opportunities/threats with the potential to affect the competitive situation of the company.

Question 3: What are the major companies that have demonstrated absorptive capability to benefit from a stock of knowledge in the erectile dysfunction market?

Today, in the information society, we live in a chaotic environment caused by the increasing interconnectedness and interdependence among people, corporations and countries. The theoretical and empirical literature about innovation suggests that patent citations are a way to evaluate the flow of knowledge from an original "stock" and therefore demonstrates imitation and spreading of an idea (Carolis, 2003). The rational of the scientific research that uses patent citations defines that all patents are based on knowledge developed in previous publications. Thus, if patent B cites patent A, this implies that the patent is part of the existing prior knowledge on which the invention B was constructed, but about which it has no credit (Meyer, 2000; Choi and Park, 2009; Gress, 2009). In short, patent citations reveal the network of cooperation for given technology and the informal dialogue with the exchange of information between companies and countries.

4. RESULTS AND DISCUSSION

Question 1: Through the patent data, it is possible to evaluate the discovery cycle of PDE-5 and correlate adaptive, absorptive and innovative capabilities?

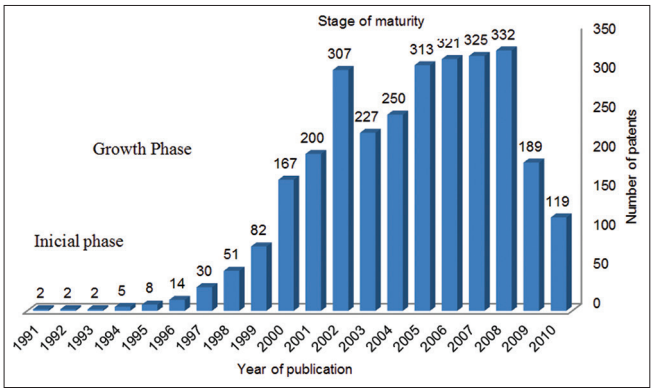
The database Derwent Innovations Index® has selected 2946 patent families classified A61P-015/10 between 1990 and 2010. These were analyzed by specific filters in a dynamic spreadsheet for counting data. To answer Question 1, it was analyzed the evolution of the number of patents classified A61P-015/10 published annually from 1990 to 2010 depending on the date of publication. It's important to point out, however, that this date represents a bias as a result of timing lag between the submission process and the granting of the application, and this fact does not invalidate the results.

In 1985, Pfizer Laboratory initiated a program of medicinal chemistry research with the goal of discovering a selective inhibitor of PDE-5 for the treatment of hypertension and other cardiovascular indications. In initial studies, the researchers used the active ingredient sildenafil citrate in the treatment of angina, a disease that causes intense pain in the chest due to lack of blood supply and nutrients to the heart (Veiga et al., 2014).

The study results were not satisfactory for angina, however, revealed a frequent side effect: Sildenafil citrate increased the volume of blood in the penis causing strong and lasting erections (Katzenstein, 1998; Pissarnitski, 2006). For this reason, the Pfizer Laboratory began in 1993 a series of studies to demonstrate the efficacy and safety of sildenafil citrate (Viagra®) in the treatment of erectile dysfunction. During a period of 4 years, Pfizer has performed 21 clinical studies involving 4500 men with erectile at a cost of 500 million dollars dysfunction. With a fanfare unprecedented in the history of medicine, Viagra® has taken the U.S. enthusiasm since it was approved on March 27, 1998 (Veiga et al., 2014).

Figure 2 illustrates that only after the technical, commercial and social consolidation of the new product that other companies were interested in the sector and the number of annual publications began to increase. Radical innovations create not only great

Figure 2: Annual number of patents classified A61P-015/10 from 1990 to 2010



Source: Search data from Database Derwent Innovations Index®

industrial possibilities but also great social uncertainties. When a radical innovation is discovered, the question becomes whether or not to accept the possible risks involved. In the case of the pharmaceutical industry, there is a risk of the products developed with the goal of improving medical service occasioning difficult to predict side effects. This problem is compounded when it comes to developing a medicine which is the first compound to be used for a given disease (Baba and Walsh, 2010). For radical innovations there is little accumulated information on the pharmacological aspects of the action of the new drug mechanism, as well as the administrative aspects in the marketing of the new medicine.

The innovative capability of Pfizer created not only a new product (technical innovation), but a new market and a new organizational structure for the company (organizational innovation/administrative). The immediate worldwide success of Viagra® could not be explained as mere effect of the massive marketing which its launch was the object. There is an assumption that it was responding to demands from powerful latent cultural-historical in a moment when it was released (Pereira, 2004; Veiga et al., 2014). The introduction of new scientific knowledge made possible the understanding of previously unconnected phenomena, which consolidated a new technological paradigm and exploitation of investigative discovery.

In a world where innovations are quickly duplicated, patenting is a relatively effective response to the vulnerability inherent in the product information. The patent does not guarantee total protection because innovation in itself reveals information which, moreover, could be protected by secrecy. In dynamic markets dominated intellectual property, the opening of the investigative content discovery provides the generalization of the concepts and the emergence of exploratory discovery. In this context, competing companies use the adaptability and absorption to create their own unique versions of "Viagra®" and to join in a proven lucrative and expanding market.

In Figure 2, the stage represented by the steep part of the curve illustrates the growth phase (1999-2002) the number of patents published about the subject. This phase represents the time when several companies identify and capitalize on opportunities in new emerging market. These companies probably abandoned products, technologies and traditional markets to develop new ways and adapt to other competitive processes. The new technology is developed within a dominant design, which enables rapid dissemination of knowledge, higher risk of overlap and smaller range of results.

After the discovery of the PDE-5 inhibitors which were effective in treating of erectile dysfunction, like Viagra® or with the potential for the same pharmacological effect chemicals were used as the basis of the mining potential active ingredients (Pissarnitski, 2006; Dimitriadis et al., 2008). So far, besides Viagra®, three other inhibitors of PDE-5 received FDA approval, Levitra® (vardanafil) and Cialis® (tadalafil) in 2003 and Stendra® (avanafil) from Vivus lab in 2012. More recently, however without expression and without international licensing by the FDA, were released three more incremental innovations for erectile dysfunction: The Zydena® (udenafil) from Dong A Pharmaceutical Co. Ltd., approved in Korea and the Russian Federation (Kim et al., 2010; McNamara and Donatucci, 2011), the Helleva® (lodenafil) Laboratory Cristália approved in Brazil in October 2007 (McNamara and Donatucci, 2011) and the Mvix® (mirodenafil) recently licensed in South Korea (Choi, et al., 2010; McNamara and Donatucci, 2011).

For the treatment of erectile dysfunction there is no "ideal drug." In fact, there are options that can suit each individual profile. Incremental innovations offered for men more treatment options orally, however, they all share the same mechanism of action of Viagra®: Are inhibitors of PDE-5. The scientific papers published so far do not support differences in efficacy between the different PDE-5 inhibitors, with contraindications and safety criteria also similar for all class representatives (Fazio and Brock, 2004; Stief et al., 2005; Hatzimouratidis and Hatzichristou, 2008; Morales et al., 2011).

Figure 2 also illustrates the phase of market maturity of PDE-5 (2003-2008). At this stage, the potential of the new technology have already been extensively explored, with possibility only minor scientific advances. Finally, the curve ends with a descending segment characterized by a drastic reduction in the number of publications (2009-2010), which suggests a declining trend. Currently, the market of erectile dysfunction is divided among several companies. In some countries is significant participation of national companies and producers of generic and similar market. Despite being divided, the market of products for the treatment of erectile dysfunction is still booming as the use of PDE-5 inhibitors today represents the first therapeutic option (Fazio and Brock, 2004; McNamara and Donatucci, 2011) and new patients are fed daily in this market.

Despite of Figure 2 shows a steadily declining for patents related to PDE-5, only in 2009 and 2010 were published 308 patents related to the subject erectile dysfunction, which suggests that research remains. New medicines are strong candidates to reach the market soon as bremelanotide, SLx2101 and its active metabolic SLx2081 (Hatzimouratidis and Hatzichristou, 2008; Kim et al., 2010; McNamara and Donatucci, 2011). Among the new drugs studied, only bremelanotide represents a new class of

treatment for erectile dysfunction. Apart from the different action mechanism involving the melanocortin receptors, this new product may be administered nasally or subcutaneously. This new drug may generate a break of concepts with a radical reconfiguration of the old system. Experimentation with new elements allows testing new possibilities. If they perform better, it can be incorporated in the established capabilities and generate a new round of investigative discovery. Despite expectations, the potential role of bremelanotide in clinical practice remains in dispute (Hatzimouratidis and Hatzichristou, 2008; Rosen et al., 2004).

For Figure 2 comes to present an increasing segment in the number of annual publications, the phase of exploratory findings should be totally inconsistent with the emerging new. At this stage of consideration, the complexity increases and provides insights and incentives for the creation of a new paradigm with great architectural change of the current system.

Question 2: What are the major companies that have demonstrated adaptive capability to identify and capitalize on opportunities in the erectile dysfunction market?

To assess the second research question, Excel® filters were used for all data related to the "depositor" field. Importantly, this analysis was performed manually on the basis of patents that had more than one depositor, since all those responsible for the deposit were considered in the evaluation. For this reason, this initial analysis included 9303 depositors, given that each patent family had on average 3 depositors.

The selection of the depositor as "government institution" was due to the presence of some suggestive terms such as hospital, school, university, institution and research foundation. Data were grouped considering the organization's name variations and available in descending order by the number of publications. A share of 95% (8871 deposits) of private institutions, including individual deposits, and 5% (432 deposits) of government institutions has been recorded.

Private pharmaceutical companies contributed the most patent applications in the erectile dysfunction market between 1990 and 2010, without considering mergers/acquisitions and contributions from subsidiaries are listed in Figure 3. The companies responsible for Viagra® (Pfizer), Levitra® (Bayer Schering Pharma) and Cialis® (Eli Lilly & Co.) are among the 10 largest depositor's private companies. Overall, the results of this analysis showed intense "spray" of deposits from individual depositors and intense concentration among private companies.

The analysis of a company's patent provides a more dynamic picture of the interest of the corporation and allows locating a target company for acquisition, merger, or other marketing activity (Narin et al., 1984). Wyeth Research on PDE-5 inhibitors may have contributed to defining the Pfizer acquisition of Wyeth, regulated by government authorities in 2009 process. Additionally, PDE-5 inhibitors are a promising target for new treatments and many companies have made researches in this field. The company Merck & Co., for example, has entered into a co-promotion agreement for the commercialization of Daxas® (roflumilast), daily administration of a medicine for patients with chronic obstructive pulmonary disease.

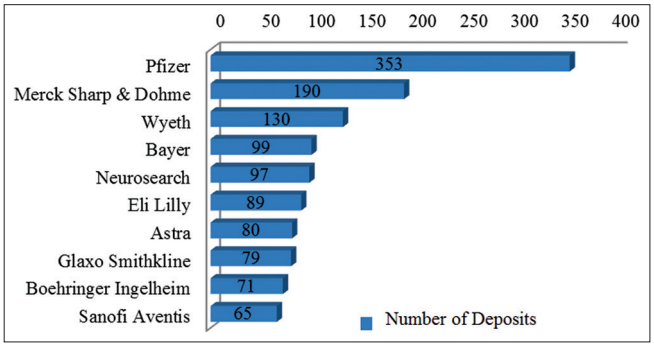
Government institutions which have most contributed with applications in the erectile dysfunction market between 1990 and 2010 are cited in Figure 4. They were the society and board of research and applied science in Paris, the Institute of Medicine of Beijing, the U.S. Department of Health and Human Services, the Institute of Pharmacopoeia of Shanghai and the University of California. In general, the results demonstrate that there is a greater number of deposits of private companies that patent governmental institutions. Basic researches conducted at research institutions are vital for investigative and exploratory discovery. However, as basic research not always has the commitment to efficiency/financial performance and strategic exploration, is the industry who actually seeks to develop adaptive capability to respond to external market opportunities for product (Angell, 2008).

Question 3: What are the major companies that have demonstrated absorptive capability to benefit from a stock of knowledge in the erectile dysfunction market?

To answer Question 3, the patent families were analyzed qualitatively and quantitatively as to quote backward[2]. For each patent family determined the total number of backward

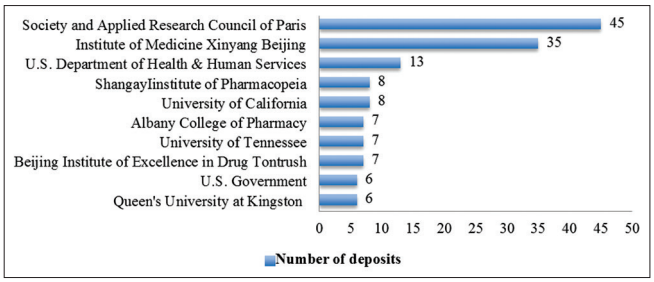
2 Quote Backward: the references of a patent come from other patent's citations temporally.

Figure 3: Private pharmaceutical companies contributed the most patent applications in the erectile dysfunction market between 1990 and 2010



Source: Search data from Database Derwent Innovations Index®

Figure 4: Governmental institutions contributed the most patent applications in the erectile dysfunction market between 1990 and 2010



Source: Search data from Database Derwent Innovations Index®

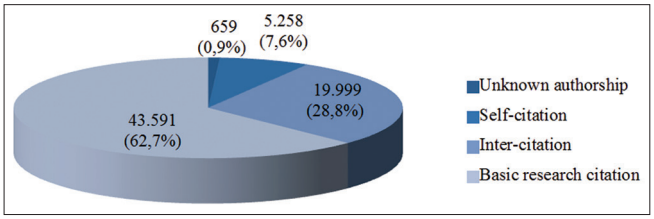
citations excluding repeated patent and those belonging to the same family. They were used only patent information inserted through the examiner, thus, it seeks to avoid the bias due to the lack of relevant prior information that the applicants not found or is not willing to reveal. Citations were counted and classified as: (i) Self-citation, when the company cited a patent filed by itself, (ii) inter-citation, when the company cited a patent filed by another transferee, (iii) quote from basic research involving the recording of scientific articles and deposits from Universities and, (iv) citation of unknown authorship, not located at Derwent Innovations Index®. The result of this analysis is illustrated in Figure 5 and shows that 62.7% of patent citations referring to basic research, 28.8% came from inter-citation, 7.6% self-citation, and 0.9% unknown authorship.

In interpreting these data, it is important to emphasize that, contrary to what has been practiced for citation counts, the program used did not have the tools to distinguish items repeated for each patent of the same family. In addition, the articles did not have a standard bibliographic reference, in turn, in many cases, difficult to assess whether it was a scientific publication. For this reason, the data regarding the percentage of citing basic research may be overestimated. For larger companies, articles and citations of other patents were manually dissected. The result of this analysis shows that the share of basic research (articles) in citing patents ranged from 50.23% (Pfizer) to 2.11% (Neurosearch) among the biggest companies. In every case, the number of articles cited exceeded the number of citations from other patents.

This result suggests a strong relationship between science and technology as the knowledge base for families in patent analysis are derived mainly from basic research. To develop the absorptive capability of external basic knowledge and convert it into products, industry researchers often work in partnership with basic research laboratories (Angell, 2008). However, it is not only through the absorption of basic knowledge that begins an exploratory discovery. Data in Figure 5 shows that companies also use the knowledge absorption from other companies (inter-service) and a "stock" of knowledge itself (self-service) for the development of new products.

For 10 private companies with the greatest number of publications in the erectile dysfunction market (1990-2010) two indexes intended to measure the absorptive capability of internal knowledge (IAC) and the absorptive capability of external knowledge (EAC) were developed. For the calculation of each index was considered

Figure 5: Percent shares of self-citation, inter-citation, basic research citation and unknown authorship in patent families of erectile dysfunction market between 1990 and 2010



Source: Search data from Database Derwent Innovations Index®

the total number of published patents (2946 patents) and the count of self and cross-citations for A61P-015/10 and subclass for each depositor.

$$EAC = \frac{\text{Percentage of company inter-quote}}{\text{Percentage of inter-quote to the subclass A61P-015/10}} \quad (1)$$

Equation (1) was based on the activity index as described by Narin et al. (1984). Thus, EAC is a ratio of percentages and their results vary around "1.00." Numerically higher values of EAC correspond to a higher degree of external knowledge embedded in publications of a given organization, in the present study. Higher values of EAC suggest that the organization uses higher capacity to absorb external knowledge for the generation of their inventions. The results obtained by application of Equation (1) are summarized in Table 1.

Table 1 shows that all businesses use a greater number of inter-citations compared to self-citations. For some of them, as in the case of Neurosearch and Wyeth, inter-quotes are three times more numerous than the self-citations. These Figures 1-5 show that the dynamics in the erectile dysfunction market capabilities are built in large part, from a "stock" of external knowledge to the organization.

From Table 1 it is also possible to note that Neurosearch and Glaxo Smithkline companies have the lowest values of EAC while Wyeth and Pfizer companies hold the greatest results. The EAC indicates that the Pfizer, for example, has 1.46 times more inter-citations in their parents considering them in a distribution proportionally in all A61P-015/10 patent subclass.

To measure the IAC index of 10 private companies with the highest number of publications in the erectile dysfunction market (1990-2010) was used in Equation (2). This considered the total number of patents (2946 patents), the total number of self-citations (5258 citations) for A61P-015/10 subclass, as well as the number of self-citations for each depositor. Similarly to EAC, IAC is a ratio of percentages and averages around "1.00." Generally, higher values of IAC represent higher percentage of insider knowledge use in the publications of a company within the scope of this study. The results obtained by application of Equation (2) are summarized in Table 2.

$$IAC = \frac{\text{Percentage of self-citations of a company}}{\text{Percentage of all self-citations to A61P-015/10}} \quad (2)$$

Table 2 shows that, in general, all companies use internal knowledge for exploring innovations in the same therapeutic field. The results ranged from 0.81 to 2.34, with high values of IAC for Pfizer, Wyeth, Eli Lilly companies and low results for Neurosearch and Glaxo Smithkline companies. The first index EAC measures the diffusion of knowledge and use of external information to the organization. IAC, in turn, evaluates the use of an internalized knowledge and its use in related areas of technology. However, the comparison between Tables 1 and 2 does not reveal a complementary result which makes the reading that the higher the

Table 1: Index of EAC on application of Equation (1)

Company	Total of patents	Total of citations	Inter-quotes	Self-citations	EAC
Pfizer	168	2365	1663	702	1.46
Merck & Co.	123	1045	654	391	0.78
Wyeth	60	1100	870	230	2.14
Bayer	60	654	478	176	1.17
Neurosearch	98	567	426	141	0.64
Eli Lilly	68	670	435	235	0.94
Astra	53	389	271	118	0.75
Glaxo Smithkline	76	480	337	143	0.65
Boehringer Ingelheim	28	274	190	84	1.00
Sanofi Aventis	50	409	290	119	0.85
Standard deviation	41.07	613.95	435.24	186.54	0.46

EAC: External absorptive capability

Table 2: Calculation of IAC through application of Equation (2)

Company	Total of patents	Total of citations	Inter-quotes	Self-citations	IAC
Pfizer	168	2365	1663	702	2.34
Merck & Co.	123	1045	654	391	1.78
Wyeth	60	1100	870	230	2.15
Bayer	60	654	478	176	1.64
Neurosearch	98	567	426	141	0.81
Eli Lilly	68	670	435	235	1.94
Astra	53	389	271	118	1.25
Glaxo Smithkline	76	480	337	143	1.05
Boehringer Ingelheim	28	274	190	84	1.68
Sanofi Aventis	50	409	290	119	1.33
Standard deviation	41.07	613.95	435.24	186.54	0.54

IAC: Internal absorptive capability

EAC, lower the IAC or *viz*. Results do not allow asserting those companies which uses less external knowledge perform better than internal knowledge in its innovations. Nevertheless, scientific studies show that the degree to which a company is based on own knowledge (measured as self-citations in their patent) provides innovations (McMillan et al., 2003). In agreement with these studies, the companies responsible for Viagra® (Pfizer), Levitra® (Bayer) and Cialis® (Eli Lilly) are among the largest IAC.

5. CONCLUDING REMARKS

A short historical review demonstrates that the establishment of the global pharmaceutical industry has overcome the challenge of researching and producing innovative products to meet the basic needs of the population medicines. Advances in science and technology play a primordial role to overcome the many necessary challenges in patient care, and to ensure the future of the pharmaceutical industry. Be assured by increasing the portfolio through mergers and acquisitions or through internal and/or external R and D, the pharmaceutical industry needs to sustain its growth through technological innovation.

In recent years, low productivity of R and D, high development costs and high failure rates have increased pressure on pharmaceutical organizations (Cuatrecasas, 2006). They face an urgent need for more effective R and D, which deliver successfully new innovative medicines. In this globalized, volatile and turbulent organizational environment, creating value may arise from the ability to configure functional skills strategically, thus involving the perception of the environment, the generation of knowledge, coordination of activities and integration of resources (Teece et al., 1997).

For the pharmaceutical industry, the dynamic capabilities are the result of co-evolution of internal and external forces (Jacobides and Winter, 2005) and this ability to integrate the environmental dynamics and the subjective internal forces emerges as a distinctive organizational capability (Lorenzoni and Lipparini, 1999). In this sense, the dynamic capabilities provide theoretical support for the claim that the company's performance is directly linked to their efforts to: (i) Recognize the value of new external information and applies them to a commercial purpose, (ii) introducing changes in the organization to create new opportunities and to better exploit existing ones, and (iii) identify and capitalize on opportunities in emerging markets.

The present study showed that these three components of dynamic capabilities, absorptive capability, innovation and adaptation, can be identified and detailed in the product discovery cycle of Viagra®. The analysis also evaluated the transition from investigative discovery to exploratory one of incremental innovations, as well as the identification of the phases of consolidation, generalization, differentiation and retribution. Furthermore, the study answers two other research questions and identifies the leading companies with adaptive and absorptive capability in the erectile dysfunction market from 1990 to 2010.

The analysis of the erectile dysfunction market confirms that technological inventions arise to meet a need and/or the discovery of a phenomenon (Arthur, 2007), i.e. the change of technological

paradigm is initiated with the intention of solving a problem, as well as inventions are shaped by social needs and respond to economic opportunities and the perceived risk. Viagra® product represents a radical innovation with major disruptive effects on the pharmaceutical market. In this particular situation, the changing technology should be seen more as an evolutionary process than a revolutionary since the discontinuity is probably due to the impact of innovation on economic and social context, not just for its radical nature (Santos, 2003).

As can be detected for several segments of the pharmaceutical industry, where a new set of technological trajectory forms, it dominates the subsequent technological and commercial development, which begins with the exploratory discoveries. This process is of extreme interest to researchers of pharmaceutical companies who want to strengthen their market position by exploiting their own leadership or the operation of the leadership of its competitors. However, not all companies are able to develop dynamic capabilities necessary for competition.

The pharmaceutical industry in the erectile dysfunction market is a highly concentrated economic sector with much of publications belonging to only 10 large companies, certainly, they have used better the market opportunities and external product by adaptive capability. In relation to available commercially medications, the market shows like oligopolistic with the participation of only three companies among the holders of medicinal products for global brand: Pfizer, Eli Lilly and Bayer Schering. These companies, in addition to adaptive capability, are characterized by innovativeness (radical or incremental) and the absorption capacity, demonstrating the need for balance between the elements of the dynamics for the achievement of competitive advantage capabilities. The results also demonstrate the negligible participation of universities and public research institutions in granting patents, but confirm the need for basic research as fundamental to the development of new medicines.

Finally, the study confirms the existence of a stock of knowledge between the pharmaceutical companies of erectile dysfunction medicine market, as well as a large absorptive capability for all of them. Comparative scientific papers between these various medications do not support large differences between PDE-5 commercially available. In fact, today, the research addresses the growing fragmentation of the innovation process so companies need external expertise and third-party patents for inventive effort, which makes the results of different companies are quite similar. Furthermore, strategic alliances between companies have become instruments to establish complementarities between their skills and essential capabilities. In this context, the logic of mergers is clear a tendency to gather in the same company the expertise and ownership of intangible assets invested in different markets and segments (Brocas, 2003; Cloodt et al., 2006; Higgins and Rodriguez, 2006).

In short, one can say that the process of pharmaceutical R and D is an uncertain, multifaceted and highly complex, which requires a strong interaction of sources of various origins. In this sense, the development and the balance between the three elements of dynamic capabilities are key elements for achieving innovation through joint efforts. The findings of this study, their interpretations and suggestions for practical implications should be considered in the context of the limitations of this study. The study looked at only a small segment of the pharmaceutical industry within a limit time. The same procedure adopted here can be applied in other pharmaceutical markets, as well as in various industrial sectors and at different periods. This is a complex subject and this study was not intended to exhaust it.

The data used in this study also represent a limitation to the study. Patent data do not cover all inventions because not all meet the criteria for patentability. Moreover, the protection provided by intellectual property has changed significantly in recent years, making the most likely companies to register patents and covering areas not previously considered. The combination of increased access to information, coupled with the increasing number of patents granted and the fact of each one, currently, has more quotes suggests a kind of "inflation" citation. Despite these limitations, the patent data should not be discarded as a statistical indicator since they provide information not catchable by other sources.

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