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"R&D AND PATENTING IN THE PHARMACEUTICAL INDUSTRY: THE INDIAN CASE AT A GLANCE"

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Firma dello studente

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Ai miei cari e a tutti coloro che

mi hanno sempre sostenuto.

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INTRODUCTION

In the 2017 "Ten years in public health" report redacted by the World Health Organization (WHO), it was estimated that nearly 2 billion of people in the world had no access to fundamental medicines, "effectively shutting them off from the benefits of advances in modern science" as declared by the ex-General Director of WHO, Dr. Margaret Chan[1].

Lack of access to medicines causes misery and suffering: no cure for a child's painful earache, women who unfortunately die during childbirth, casualties from diseases that are quickly and inexpensively prevented or cured. People in lower-income countries suffer from diseases going from the so-called "neglected tropical diseases"[2], for instance, Dengue, Leprosy, Malaria, to a multitude of infectious diseases that in the First World are uncommon, such as HIV, Hepatitis B, Pneumonia, that every year kill millions. Lack of access to medicines is one inequality that can be measured by a starkly visible yardstick: numbers of preventable deaths (World Health Organization, 2017).

This complex and vexing problem has been vastly explored, with an extensive literature on access to health and medicines, starting from income inequality, sustainable devolvement, exploitation of the poor, market failure, and other economic and social arguments. In this thesis, we will focus the attention to this issue from a different standpoint, which is perhaps one of the primary reasons for the difficulty for poor people to get affordable medicines: the Pharmaceutical Patent's system.

The International Patent's system that, at the moment, is in force in all the countries that are part of the World Trade Organization (WTO) is the Agreement on Trips-Related Aspects of Intellectual Property Rights (TRIPS). This International legal agreement sets down minimum standards for the regulation by the WTO members of many forms of intellectual property, the most important being Patents. This agreement allows an inventor, for example, a pharmaceutical company that invented a new formula for a drug, to enjoy the protection of a minimum term of 20 years from the filing date of the patent application for that formula, virtually guaranteeing a monopoly on the product for at least two decades. This duration hinders the free market on medicines, implying that the most influential companies in the world, which also have much more investment capacities in R&D with respect to small companies that operate in lower- and middle-income countries. Indeed, this kind of protection was put in place

[1] Interview available at: https://www.who.int/publications/10-year-review/dg-letter/en/
[2] For the complete list of the diseases: https://www.who.int/neglected_diseases/diseases/en/

to safeguard any inventors, allowing them to secure a fair amount of time to gain a profit on their investment and effort.

Nevertheless, pharmaceutical companies exploit this insurance and strategically apply for many patents on a single drug, just making minor changes on the formulas, a procedure called "Evergreening", de facto canceling any competitors. Humira, the best-selling drug in the world, brought the company that produces it almost 20 billion $ in global sales in 2018 (Mukherjee, 2019), and is protected by over 240 patents, with all of them differing slightly from each other (I-MAK, 2019). This medication is used to treat different forms of arthritis and costs nearly $3000 per unit[3]. Does the expense that the company had incurred before patenting the formula justify this cost? What if an individual from a lower-income country has no financial capacity to buy such an expensive drug and still needs it? Is it fair that a company ultimately decides the lives of people that to them does not exist?

In chapter one, we will assess the Agreement on Intellectual property, expanding on Patents, trying to find how they are valuated, and the different approaches that are currently being used for their economic evaluation.

In chapter two we will focus on the relationship between the TRIPS Agreement and the drugs industry, studying how pharmaceutical firms manipulate the market using the Agreement's provisions. We will also underline the differences between the European and Indian current situation, both in terms of the industries' characteristics and the patent systems peculiarities.

Finally, in chapter three, we will present an empirical analysis where we use data from the EU R&D Survey containing various numerical information on the first 500 enterprises in the world in terms of research expenditure, and patents data from the EPO, to answer the main question of our thesis: is a model based on a strict patent system, such as the Indian one, able to stimulate research and therefore applicable to more modern industries, like Europe? In other terms: is a model that puts the public interest first rather than the interests of Big Pharma, able to represent an efficient and right example for the richest countries in the World?

[3] Source of the price: https://www.drugs.com/price-guide/humira

CHAPTER ONE: TRIPS, PATENTS AND VALUE OF PATENTS

1.1 What is TRIPS

Before the 19th century, intellectual properties rights (IPRs) were not considered a matter of international and intergovernmental discussion and their regulation were just a strict national concern. Although, during the 19th century, IPRs was the major subject of various international agreements[4], striving for an enhanced international harmonization, they all suffered from the mistake of not specifying minimum standards for patent protection, causing them rather unsuccessful (Descheemaeker, 2012). In countries like the US and UK, IPRs have not only been patentable since the 18th century, but some of them (like pharmaceutical patents) received a special treatment, with a powerful protection for both processes and products. On the other hand, there were countries, especially developing and lower-income ones, that did not strive to create a very rigid intellectual properties rights system.

After decades of diverging ideas, the Agreement on Trade-Related Aspects of Intellectual Property Rights, better known as TRIPS, was negotiated, under strong pressure by industrialized countries, between 1986 to 1994, during the Uruguay Round of the General Agreement on Tariffs and Trade (GATT) and successively entered into force in 1995. As one of the World Trade Organization (WTO) agreements, it was immediately binding for the WTO at the time, and for the future members, who had to accept it to enter the Organization. The TRIPS Agreement is the first and the most comprehensive WTO requiring Members to establish a relatively detailed set of substantive norms within their national legal systems, and at the same time requiring them to put in place enforcement measures and procedures meeting minimum standards. Specifically, the rights that are legally guaranteed by the Agreement are: copyright and related rights, trademarks, geographical indications, industrial designs, integrated circuits, undisclosed information and the most relevant, patents.

TRIPS attempt to define an equilibrium between the long-term social aim of providing incentives for future inventions and creation, and the short-term aim of allowing people to use existing inventions and creations (World Trade Organization, 2006).

However, adding to the fact that TRIPS has been sometimes referred to the first WTO agreement that prescribed “positive law” (United Nations, 2003) before its entry into force had

[4] 1883, Paris Convention; 1873, Vienna Conference; 1970, Patent Cooperation Treaty; 1973, Munich Convention; 1975, Community Patent Convention

generated a considerable amount of controversy among the WTO members, particularly caused by the contentious between developed and developing countries.

As mentioned before, the TRIPS established minimum standards for nearly all forms of IP, obliging Members of the WTO to provide protection for any sort of invention, whether it is a product or a process, in all field of technology, provided that the invention is new, involves an inventive step and is capable of an industrial application. TRIPS incorporated also various public benefit safeguards, for example public-health, allowing sufficient flexibility for countries to take their own intellectual properties systems and developmental needs into account and preventing the abuse of rules. Both minimum standards and public safeguard were the pillar of the TRIPS, which at the time were sufficient to consider it as the most important Trade Agreement of all time.

The Agreement is composed by seven parts. The first two parts are concerned with rules that WTO Members are expected to implement and apply in their national legal systems. The third part lists the enforcement obligations of Members, and the fourth establishes the means for acquiring and maintaining intellectual property rights. The fifth parts is reserved to dispute settlement under the Agreement while the sixth and the last parts concerns transitional arrangements and other matters. Since in this thesis we take our focus on patents, in the following paragraphs we'll review some of the relevant articles regarding them.

In particular, our attention goes to Part II, Section 5, of the TRIPS Agreement[5] (World Trade Organization, 1994), starting from Article 27 on Patentable Subject Matter where is stated that patents can be available for any inventions, both product and processes, if and only if "[…] they are new, involve an inventive step and are capable of industrial application". It is specified in a comment that the terms "inventive step" and "capable of industrial application" can be interpreted as synonyms of "non-obvious" and "useful" respectively. It appears that a patent must be characterized by three key attributes, which are of course subject to personal interpretation. In Article 27 are also stated the reasons for excluding from patentability some inventions with the principal one being for the "[…] prevention within their territory of the commercial exploitation of which is necessary to protect public order or morality".

Article 28, titled "Rights Conferred" shows the exclusive right reserved to a patent owner thanks to which she can prevent third parties not having her consent from the acts of: "[…] making, using, offering for sale, selling, or importing for these purposes that product". Also, "Patent owners have the right to assign, or transfer by succession, the patent and to conclude licensing contracts". Article 30, on "Exceptions to Right Conferred" consider the possibility

[5] For the full document: https://www.wto.org/english/docs_e/legal_e/27-trips.pdf

that patents exclusivity rights may be limited, only if they "[…] do not unreasonably conflict with a normal exploitation of the patent and do not unreasonably prejudice the legitimate interests of the patent owner, taking account of the legitimate interests of third parties".

For what concerns the "Conditions on Patent Applicants", Article 29 requires that an applicant has to "[…] disclose the invention in a manner sufficiently clear and complete for the invention to be carried out by a person skilled in the art" and "[…] the best mode for carrying out the invention".

Article 31 titled "Other Use Without Authorization of the Right Holder" includes all the provisions that have to be respected when a law of a Member of the WTO allows the use of a patent invention without the authorization of the right holder. First, such use is permitted only if "[…] the proposed user has made efforts to obtain authorization from the right holder on reasonable commercial terms and conditions and that such efforts have not been successful within a reasonable period of time". This requirement may be waived by a Member in case of national or any extreme urgency, or in cases of public non-commercial use. In both cases, the right holder shall be informed promptly before the actual use of the patent. The scope and duration of such use is limited to the purpose for which it was given authorization, and such use must be non-exclusive and non-assignable. The use shall be authorized mostly for the supply of the domestic market of the authorizing Member and shall be liable "[…] to be terminated when the circumstances which led to it cease to exist and are unlikely to recur". The patent holder must be adequately remunerated considering the economic value of the authorization. Also, the legal validity regarding the decision about the authorization and the remuneration "[…] shall be subject to judicial review or other independent review by a distinct higher authority". Members can avoid to apply the previous conditions when "[…] the use is permitted to remedy a practice determined after judicial or administrative process to be anti-competitive". Finally, when the exploitation of a patent ("the second patent") cannot be exploited without infringing another patent ("the first patent"), the following conditions apply: the second patent involve an important technological advance with respect to the first patent, the first patent owner "[…] shall be entitled to a cross-licence on reasonable terms to use the invention claimed in the second patent", and the authorized use for the first patent is non-assignable "[…] expect with the assignment of the second patent".

Article 32 states that any decision to revoke or forfeit a patent after a judicial review shall be available. The most important provision contained in the TRIPS Agreement is with no doubt Article 33, which indicates that "The term of a protection available shall not end before the expiration of a period of twenty years counted from the filing date". The last Article on the section dedicated to patents is Article 34 titled "Process Patents: Burden of proof". In particular,

if the patent is a process for obtaining a product "[…] the judicial authorities shall have the authority to order the defendant to prove that the process to obtain an identical product differs from the patented process".

The TRIPS Agreement significantly potentiated the protection of Intellectual Property Rights by requiring all Member to establish a minimum 20-year period protection in all field of technology. Nonetheless, this treaty was strongly opposed by developing countries that did not have a strong IPRs system, especially for patents in certain areas of technology, such as pharmaceutical formulas, so they had to comply with TRIPS, amending their laws.

In addition, TRIPS allows Members to use measures such as compulsory licences, parallel imports and exceptions to patent rights, and also to strengthen the patentability criteria. These systems have been put in place to balance IP rights with public needs (especially health-related needs) and they can be used to increase competition and protect consumers.

The main implication on public health that the TRIPS brought in at the time, was that the generic drugs production was somehow at risk in under-developed countries, which did not have a strong patent system. Right after the Agreement entered into force, the flexibilities mentioned before were challenged by international pharmaceutical companies and governments of developed countries that wanted to secure the monopolies that the patent system provided them. The continuing fights between the parts involved, led to the Declaration on TRIPS, which was adopted on the 14th of November 2011, during the 4th WTO Ministerial Meeting at Doha, Qatar (World Trade Organization, 2001)[6]. The main reason for the existence of this declaration was to promote a balanced interpretation and implementation of the provisions of the TRIPS Agreement in a way such that it is supportive of a WTO Member's right to protect public health and ensure access to medicines for all (South Centre, 2011).

The Declaration, divided in 7 points, recognizes the gravity of public health issues afflicting many developing and under-developed countries, in particular those where HIV/AIDS, tuberculosis, malaria and other serious epidemics are causing a huge number of deaths. For this reason, in the Declaration, it is indicated that the provisions established in the TRIPS Agreement can be used with the maximum flexibilities. In addition, in point 5 of the Declaration, some TRIPS provisions have been better clarified. For example, WTO members has the right to grant compulsory licences and to determine what makes up a national emergency or other circumstances of extreme urgency. Developed-countries are encouraged to provide incentives to their enterprises and institutions to transfer technologies to least-developed countries, which are also exempted, with regards to only pharmaceutical patents, from applying Section 5 and 7

[6] For the full Doha Declaration official document:
https://www.wto.org/english/thewto_e/minist_e/min01_e/mindecl_trips_e.htm

of Part II of the TRIPS Agreement, until 1 January 2016 (the date has been later extended to 1 January 2033). With the last decision, a major barrier to access to affordable medicines, for poor countries have been removed.

Having described the fundamental structure of the TRIPS Agreement, from the next section, we will solely focus on patents, starting from a general economic theory on patent rights.

1.2 Economic background on patents

According to the World Intellectual Property Organization (WIPO) a patent "is an exclusive right granted for an invention, which is a product or a process that provides, in general, a new way of doing something, or offers a new technical solution to a problem. To get a patent, technical information about the invention must be disclosed to the public in a patent application" (WIPO, 2020).

This definition clearly shows that it is a right (even though only a temporary right), but not a guarantee to exclude others from making, using, or even selling the patented property. For what concerns the disclosure to the public of the patent application, there are some interpretation differences between Europe and the USA, but it is safe to say that the disclosure should be viewed as broadly helpful to third parties wishing to understand the nature of innovation (Rockett, 2010). Patentable subject matter can vary a lot: they can be a process, a product, a composition of matter, a machine, or a new and useful improvement of any of these. In addition, in almost all the patent systems, a patent application is required to provide a significant innovative step. Finally, a patent right, after being granted, can be exercised, traded, sold or abandoned, just like all forms of property rights.

From an economic point of view, the crucial characteristics of patents are that they function in conjunction with knowledge, an intangible asset, as embodied in an innovative product or process, and they confer monopoly rights to the inventor (Langinier & Moschini, 2002). Whenever there is creation new knowledge that makes the production of new products or processes possible, it obviously brings considerable economic value to the table, but it has features that make it problematic for the market system to handle it properly (Arrow, 1962). According to the Arrow Model, knowledge is a quintessential public goods and they are non-rival in consumption, meaning that the consumption of a public good by one individual does not reduce the amount available for others. Public goods are also non-excludable, which means that it is not possible to prevent people from enjoying the public good once it is available. With these two features in mind, it is clear why a competitive system has some issues with public goods. Indeed, when an inventor bears all the cost of an innovation, everyone else can benefit from a discovery with zero costs, having an incentive to free ride on the efforts of others. The

free-rider problem is considered undesirable within economic markets, as businesses cannot charge for each unit of a public good that is consumed, so that there is little incentive to produce, or enhance public goods (Eccleston-Turner, 2016).

The inherent externalities associated with this class of public good generate a market failure: a competitive market system may be expected to provide an inefficiently low level of innovations (Arrow, 1962). This issue is usually addressed, in a patent system, by attacking the non-appropriability of knowledge that lies in the hearts of this market failure. In particular, by allowing innovators with the possession of property rights on their inventions, patents are legal means of influencing the excludability attributes of such a pure public good.

The most important economic benefits and costs of the patent system are closely related to the nature of the market failure that it addresses, and to the second-best character of the solution it provides (Rockett, 2010). Nonetheless, Arrow (1962), proposes an alternative solution: for optimal allocation to invention, it is necessary that the government or any other institutional entities that are not founded on profit-loss criteria to finance research and invention. The Arrow Model is based on the following five assumptions (Pompei, 2017):

1) The underlying knowledge innovation is a pure public good;
2) Innovation can actually reduce costs and innovate processes;
3) With the presence of a patent system, only one firm can innovate and apply for a patent;
4) The production process is characterized by indivisibilities and uncertainty;
5) The technological incentive (TI) to innovate is defined as:

$$TI = \pi^{post-innovation} - \pi^{pre-innovation}$$

The last formula can be interpreted as the additional amount of profit that a firm can make, thanks to the value of the innovation.

Consider now a monopoly situation: the firm innovates according to TI, that is the positive difference between the post innovation profit (blue rectangle) and the pre-innovation profit (orange rectangle), as show in Figure 1 below. By introducing a radical process innovation, the monopolistic firm not only sets the post innovation price (P'm) lower than the previous one (Pm), but P'm is also lower than the previous constant marginal cost (c).

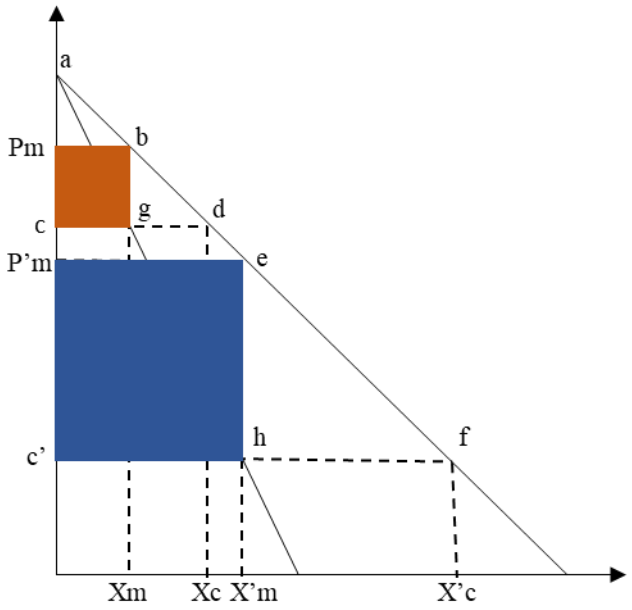

Figure 1: Innovation in a monopolistic scenario (adapted from Pompei (2017))

In the opposite scenario, so in a perfectly competitive market, many firms compete with each other, but only one can win the innovation race and get the patent approved. Here, TI is the positive difference between the post innovation profit (yellow rectangle) and zero (Figure 2). The technology innovation of a competitive firm is large than the TI of a monopolistic one, because no profits were accruing to competitive firms before introducing the innovation. Since only one firm can get a patent, this competitive market becomes a monopolistic one after the successful grant of the IP right.

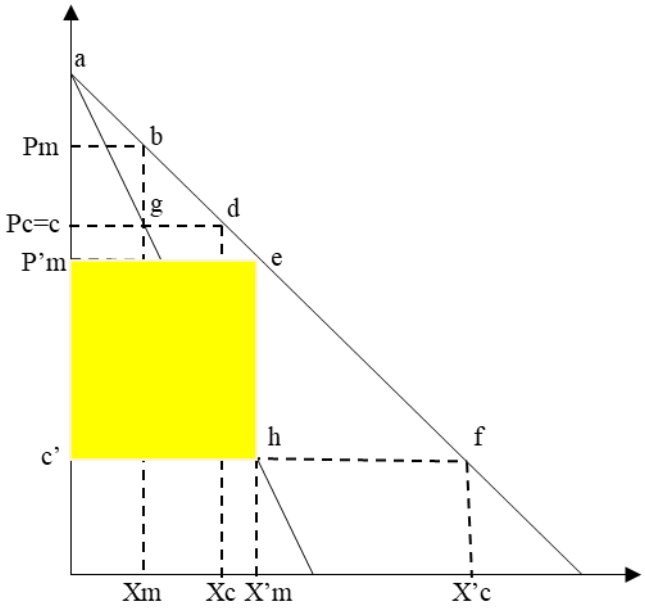

Figure 2: Innovation in a perfect competition scenario (adapted from Pompei (2017))

When the government supports innovation, through tax incentives for example a competitive market is guaranteed by the fact that firms sell all goods at a substantially lower cost. It is also impossible that any form of monopoly emerges and in definitive, the social welfare increases. The TI in this case is equal to the red trapezoid, and it is graphically obvious the increase in profit with respect to the former two cases.

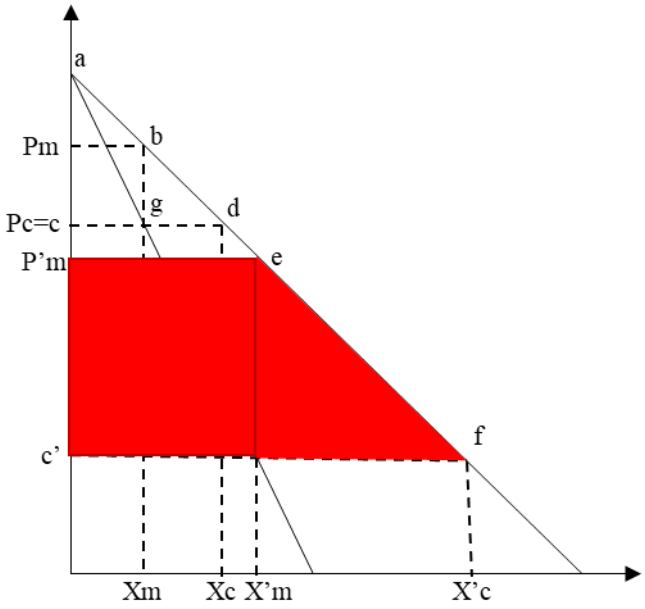

Figure 3: Innovation in the government incentives case (adapted from Pompei (2017))

The Arrow Model described so far, is one of the three patent system theories that have emerged over time. In particular, this model is based on the reward theory (the most traditional one), where innovation is considered a social good. Therefore, systems should be set up to reward innovation, and since patents perform this function, they provide exclusive rights to an invention for a defined period of years (Kitch, 1977).

The primary objective in the reward theory involves discussions about incentives, and the policies always focus on conceiving optimal incentive structures, while reducing the social costs of access restriction. In this theory is the society who has to endure the reduction in social welfare because the innovator enjoys monopoly rents. Nonetheless, society understands that these rewards are essential for innovations, so it is a compromise for the greater good (Greenspoon & Cottle, 2011). From a different point of view, it is arguable that these rewards can be unjust because those who make a small innovation may obtain the same profits of a pioneer.

Another theory that tries to better explain the interconnections among innovator competing with each other is the prospect theory (Kitch, 1977). According to this theory, a patent is a document that serves as a public announcement of an innovation that already has occurred. Consequently, the government grants the rights to the first inventor but with the open nature of the patent

document, actually an innovating firm signals to other firms what has already been invented. This incentivize others to "prospect" (e.g. to explore) in other areas, especially competitors who then can put their effort in fields that are not related to those inventions. A portfolio of patents is capable to reveal the entire direction in which an innovating firm is going (Greenspoon & Cottle, 2011). The more competitors continue prospecting for innovations across a range of ideas away from what has already been done, the more it results to further prospecting and perpetuation of the system.

Dissimilarly to reward theory, the focus of the prospect theory is on the use of patents to minimize duplication of effort among competing innovating firms. In this case, the social welfare benefits are determined considering the fact that each firm goes in its own direction with no duplicating efforts.

Last but not least, Commercialization theory faces the patent system subject from a different angle, because it focuses neither on compensating for new ideas, nor on efficiency among competing firms in resource allocation. Indeed, it directly looks at the effects of patent owners and transfer (Kieff, 2003). In this model, a patent has two characteristics: beaconing and bargaining. The former alerts the world on the technologies and rights that a patent incorporates, while the latter derives from the fact that a patent right can be transferred (Greenspoon & Cottle, 2011). These two features work together, enabling multiple actors to communicate with each other and work together within a product market.

The key characteristics of patent, in this theory, is that they can be transferred and exchanged due to the fact that each patent right owner can use it as she wishes.

From the description of different patent system theory, one question it still remains an unanswered question: what is the economic value of a patent and how can it be valued?

1.3 The economic value of patents

For all enterprises, innovation is the crucial mean to be competitive in the markets they operate in, but to have an extra gear they need to protect their innovation, keeping other companies from using the same technologies. For this purpose, patents provide businesses with the unique opportunities to keep their idea locked inside their organization (even though only for a predetermined period). Due to the fact that patents become in this way an intangible asset to companies, it is important for any potential investor, to know how to calculate a patent's value and understand the overall value of the company, based on it.

Hall (2009) states that the first step is to define what "value of patents" means. We can interpret the value in two ways: 1) as the value of the underlying invention that the patent protects; or 2) as the value of the patent right, which is the private incremental value of taking out a patent.

The second interpretation is the incentive effect of patenting, while the former is what interests us from the perspective of a social welfare system, or when we use patents as indicators of innovative activity (Hall, 2009).

According to Hall (2009), there are two different strategies for measuring patent's values. The first strategy values a portfolio of patent held by a company, using a regression of firm market value on various firm characteristics (for example, tangible assets, spending in R&D and so on) and including a measure of the patents owned by a firm. The second strategy, on the other hand, values a single patent using two opposite methodologies: the former observes the patent owner's willingness to pay renewal fees on the patent, the latter surveying its owner or inventor and attempting to elicit an estimate of its value.

The first strategy, i.e. portfolio approach, relates the financial market valuation of a firm to its tangible and intangible assets. The coefficients in a regression constructed with this strategy, are the shadow value of the various assets in the market, and not being structural parameters, they vary over time and space. Financial markets will value patents both as indicator parameters, since they are correlated with the success of innovative activity, and as instrumental variables that secure returns to that activity by excluding other competitors. Portfolio approaches will generally measure a combination of part of the value of the underlying inventions and the patent rights associated with them.

The literature on the relationship between market valuation and the firm's patent portfolio is vast. It is worth starting from the observation that much of the evidence that Hall (2009) gathered is related to Anglo-Saxon economies plus Japan, because in those country financial markets are strongly developed. The results can be summarized, noting that patents are usually traded above and beyond the R&D done by a company and that pharmaceutical patent protection value is higher than other sectors.

Measures of the quality of the portfolio, in particular the number of times a patent has received citations, are even more strongly associated than patents with firm market value: this reflect an important fact which is that most of the patents have absolutely no value, and are worthless and very few are worth a great deal. This fact does not mean that most are not needed or should not have been issued, but it suggests that the uncertainty at the time of issue of the patent rights is very large.

Using renewal data to estimate the value of a patent is the best way to analyze the problem if we are interested in the value of obtaining a patent instead of in the value of the underlying. The idea behind this assumption made by Hall (2009) is that the fees for renewing a patent rises over time, so one can get an idea of the distribution of the value of patent coverage in a particular jurisdiction by looking at how many patents are renewed at different lifetimes.

Gambardella (2013) reviews few representative papers that try to better understand the value of the patented inventions, organizing them in 3 categories each of which assessing respectively: the value of patent rights, the value of patents as quality signals, and the value of patented inventions as a whole. In the last category, the focus is on the creation of value through the number of inventions produced rather than increase in the value of individual invention.

1.4 The value of patent rights

To be able to uncover the value of patent rights, it is fundamental to start from the idea that patent "lives" are an indicator of the value itself because it is very expensive to patent holders to renew protection of additional years. The median values from patents issued in 1970 in Germany, France and UK were respectively $17,239, $847 and $1861 (Schankerman & Pakes, 1986) and since the distribution means are higher in France and the UK, it is safe to say that the data have a skewed nature (Gambardella, 2013).

Studies that make use of renewal fees, rely on the fact that a considerable number of patents is not renewed until the end of the legal lifespan, but in this case, renewal fees only provide a lower bound. Bessen (2008) estimated patent rights values using US data, assuming that the distribution of a patent right value follows a log-normal distribution. His approach combines two novel ideas. One uses data on patent renewal decisions to estimate the value of holding a patent, so the value of a patent is revealed when its owner pays a renewal fee. The other one emphasizes the relationship between patent value and a variety of patent characteristics, in particular patent "quality. These studies look at the correlations between patent characteristics and variables that should be correlated with patent value. Based on such correlations, it is possible for researchers to estimate the value of a patent from the number of times it has been cited. Nevertheless, the authors of these studies recognize that the relationship between citations and patent value is noisy (Bessen, 2008).

Patent fees, which are increasing over time, provide an observed lower bound for the value of the patent at each cutoff point in which patents need to be renewed (in the US 4,8,12 years after the first grant by the IP Office). Bessen (2008) then run an ordered probit regression using information on patents renewal (for example if they were renewed after year 4, but not after year 8, and so on). He finds that the patents granted to US patentees in 1991 were worth about $78,000 in the mean ($7000 in the median) to their owners. He estimates the ratio of patent value to R&D–a measure of the subsidy that patents provide to R&D investment–to being only about 3%. Nonetheless, the value of US patents to US owners in 1991 was more than $4 billion (Bessen, 2008). Not surprisingly he finds that there are sizeable differences in patent value across distinct groups of patentees. Small entities–individuals, small corporations, non-profit

organizations–have patent values are on average less than half as large as the values obtained by large corporations. This difference disappears in the high-tech industry where markets for technology work particularly well. Finally, he quantifies the association between litigation and patent citation statistics and patent value. Indeed, a litigated patent is worth nearly six times as much as non-litigated patent, and an additional patent citation received increases patent value by 5.5% on average (Bessen, 2008).

Another author that investigates the value of patents using renewal fees is Serrano (2011). He combines information on renewals and patent trade to get an accurate estimate of the value of patent rights. He develops and estimates a model relying on data of transfer of patents in a sample of patents applied for and granted to US small firms. The fundamental assumption is that traded patents are worth more than just renewed patents because the owner also considers the gains enjoyed by the buyers who earn more than they do from patents. First, the author finds that the mean value of patent rights in 2003 is $164,670 for traded patent and $50,162 for non-traded patents. Second, he finds that the volume of trade of patents accounts for almost fifty percent of the total value of all patents. Third, the gains from the trade of these patents represent more or less ten percent of the total volume of patents trade. Finally, the effect of lowering the costs of technology transfer by fifty percent is that the probability that a patent is traded, increases by six percent and the value of gains from trade rises by only ten percent (Serrano, 2011). Compared to Bessen (2008), he finds a smaller value of patent rights, although including only patents owned by small firms (less than 500 employees).

Another paper that relates with Serrano (2011), is the one from Galasso et al. (2011), where they study how the market for patents affects the enforcement of patent rights. Conventional studies associate the reallocation of patent rights through trade with comparative advantages in commercializing the innovation. The associated product market gains from trade should increase litigation risk for traded patents. Instead, the authors identify an alternative source of gains from trade, i.e. comparative advantage in patent enforcement, and show that this mechanism reduce patent litigation (Galasso, et al., 2011).

Hall et al. (2005) and Bessen (2009) use stock market value of the patent-owning firms to estimate the value of patent rights.

The first study shows that, besides R&D and simple patent counts, patent citations possess significant information on the market value of firms. Their findings help overcome the problem of the heterogeneity in the "importance" of patents that greatly undermined their use in the explanation of firm value or performance. They found that the marginal effect of additional citations per patent on market value is very high: if a company's patents "quality" increases, so that on average these patents receive one additional citation, the firm's market value would

increase by 3% (Hall, et al., 2005). In addition, they observed that market value is highly correlated with the portion of down-the-line citations that cannot be predicted, if past citations data are used. This confirms that the market is already aware of the value of particular innovations. Another interesting finding is that market value is positively correlated with the share of self-citations out of total citations to a firm's patents, but such relationship weakens with the size of a firm's portfolio of patents.

The second study, from Bessen (2009), shows that the standard market value equation does not provide a direct approximation of the patent premium. With his model, he is able to relate the market value of patents with the aggregate capital stock and the present discounted value of firms rents. In turn, firm rents have a direct relationship with a firm's patent portfolio, the mean patent rent, the firm mark-up for rents earned on the other assets of a company. Unfortunately, it is not possible to estimate directly the mean patent rent because patents may also account for higher quality of R&D, and thus are related to the other assets of a firm (Bessen, 2009). His estimate of the standard market value is $370,000 using US patent from 1992.

The studies mentioned so far estimate patent premiums from the behavior of firms, but ideally it would be better, according to Gambardella (2013), to compare the value of a patented invention with and without the patent. In particular, Arora et al. (2008) develop a model in which they consider the predisposition of firms to patent. They calculate that, when patenting an invention, firms expect to earn 47% more than if they had not patented it. They also show that the unconditional expectation of the patent premium is negative and equal, on average, to 40% (Arora, et al., 2008). This means that the costs of patenting for the average invention overcome its benefits.

Jensen et al. (2011) use survey data on 1,790 Australian inventions to estimate the average patent premium, both for successfully patented and unpatented inventions. Their main results are that inventions protected by a patent are 38-47% more valuable than inventions without a patent, ceteris paribus. In addition, their calculation supports the notion that inventions registered to private firms are more valuable than those registered to individuals or to public organizations.

Differently from other studies, where patents are more valuable in pharmaceuticals and chemicals areas, they found no evidence to suggest that the effect of a patent grant is different across technology areas (Jensen, et al., 2011). Finally, they found that the patent premium implies that a patent increases the value of the median invention by about A$256,000 (in 2007), and this value is bigger than those calculated by Bessen (2008) and Serrano (2012). This overestimation of the patent premium may derive from the fact that survey measures of invention value capture the full value of inventions rather than only the patent right value.

1.5 Value of patents as quality signals

Hsu and Ziedonis (2013), study entrepreneurial-firm patents to find how they play distinctive roles in different competitive areas. In particular, they consider patents having two fundamental characteristics: a) as rights to exclude others, patents serve the already mentioned role of legal safeguards in product markets; and b) as quality signals, patents could also improve access and the terms of trade in factor input markets. They provide evidence that patents confer dual advantages basing their work on data from 370 venture-backed semiconductor start-ups, founded between 1979 and 1999. More specifically, they find that patents are more influential for founders lacking prior entrepreneurial success in securing initial funds from prominent Venture Capitalists. In addition, they find that patents induce steeper valuation adjustments in earlier round of VC financing and, conditioned on an IPO exit, patents play a more influential role in bridging information gaps with public investors when start-ups lack prominent VC investors. These results are not coherent with the traditional view that patents serve a singular objective in protecting the invention from other firms, therefore they confirm that patents can also be an indicator of the quality of a firm (Hsu & Ziedonis, 2013). According to their estimation, the sample mean of pre-money evaluation is 28.5 million US dollars. With a 100% increase in patent application stock, the pre-money evaluation increases of 1.2 million USD. This enormous increase may rely on the fact that patents, during the earlier stages, provide stronger protection because they are the only instruments that enable firms to protect their inventions.

Hsu and Ziedonis (2013) suggest also that patents are costly to get. Firms face the costs of information disclosure and the opportunity cost of interacting with multiple actors, and if these costs are high enough, they discourage lower quality firms from patenting their invention. In this way, patents work as quality signals. Nevertheless, on one hand, higher quality firms may be more concerned with revealing confidential information related to their inventions, especially if they could not patent those inventions. On the other hand, higher quality firms may have better inventive capacities which makes them easier to write new patents. Lower or unexperienced quality firms, instead, face the opposite situation. Finally, the value of patents estimated by Hsu and Ziedonis (2013) is significantly higher than the estimated value of patents' rights exhibited before, even though it appears that this difference is largely present in younger firms at the beginning of their business path.

Another study that addressed patents as quality signals was the one from Hoenig and Henkel (2012). They use a conjoint-based survey among 187 European and US venture capitalists and investigate to what extent the decisions of venture capitalists are affected by start-up's patents, research alliances, and team experience as signals of the quality of its technology. They find

that no signaling effect of patents regarding the start-up's technology quality can be identified, neither of patent applications nor of granted patents. Instead, the presence of an R&D alliance seems to work as a quality signal (Hoenig & Henkel, 2012). These results challenge the evidence regarding the twofold role of patents from Hsu and Ziedonis (2013). They explain that one interpretation of their results could be that patent rights, and even more so patent applications, are relatively easy to get and therefore hardly a proof of technological quality. Even though their findings could contradict the twofold role of patents, venture capitalists might still draw implications from existing patents on other unobservable start-up characteristics, such as the know-how of the entrepreneurial team.

Greenberg (2013) also considers the impact of intellectual property on the market for entrepreneurial finance. If the market for financing start-ups were efficient, the valuations of them by investors would be independent of whether their patents were pending or granted. However, she finds that asymmetric information and adverse selection both lower valuations, because of the interconnections between patents and firms' values perception. Using data from 317 Israeli technological start-ups, she shows that the granting of patents positively affects investors' perceptions of firm value for early stage or young start-ups (Greenberg, 2013). This finding is consistent with the view that the mitigation of uncertainty about the scope of intellectual property protection enhances information disclosure by entrepreneurs and reduces asymmetric information and adverse selection in the market for entrepreneurial finance (Arrow, 1962). In addition, patent grants are significant only for new ventures, during early financing rounds and in pre-revenue stages, to support the theory that patent rights are more important to companies that lack other mechanisms to prevent the expropriation of their ideas. These mechanisms become more available to firms as they mature and establish proven track records. This study also shows that patent grants influence start-ups' ability to obtain financing from external resource providers.

1.6 Value of portfolios of patented inventions

Trajtenberg (1990) states that the use of intellectual property in economic research, specifically patents, has been hindered because patents vary enormously in their importance or value, so simple patent counts cannot be enough to be informative of innovative output. Nonetheless, he successfully demonstrated, with a pioneering work, that patents' citations are correlated with their intrinsic economic value (Trajtenberg, 1990).

Another study on patents' citations is the one from Harhoff et al. (2003) where they, for the first time, used patent surveys to assess the economic value of patents. The data they use in the paper, come from a survey of German patent-holders who assigned monetary value to

particularly important patents. They established that several indicators are significantly correlated with patent value. Among these indicators, of course citations, but also references to the patent literature, and positive outcomes of legal opposition. For what concerns the latter, the bigger is the value of the patent, the stronger will be the likelihood to be attacked. In survey-driven studies such as this one, the authors are able to capture the full value of the patent right (Harhoff, et al., 2003). This is because, according to Gambardella (2013), unlike renewal fees, or other studies before mentioned, here the question (on the survey) asks for the minimum price at which the owner is willing to offer the patent to a competitor.

A relevant study that aims to measure the economic value of patent portfolios is the one from Gambardella et al. (2017). The novelty of their analysis comes from the fact that they look at patent portfolios related to a particular invention rather than at the level of the firm as a whole. Their work separates the economic value of efforts directed toward an individual patented invention in the portfolio and the economic value of expanding the number of inventions to form larger portfolios. They find that the resources invested in individual inventions exhibit diminishing returns, and that the elasticity of value with respect to portfolio size is quite big. Obviously, the more effort you put in an invention, the more its technical value will increase. Nevertheless, from an economic point of view, these efforts are not directly linked to a much higher economic value. In the author's opinion, value arises from the combination of the inventions' peculiarities. The result of this is that resources invested in individual inventions exhibit diminishing returns, therefore firms should redirect their efforts into developing a valuable portfolio of patents, and as a result increasing the value of their inventions (Gambardella, et al., 2017). This increase may be because of stronger protection created by dividing an invention into separated patentable components, or because of synergies in value.

From another perspective, the value of the portfolio can be described as the product of the number of patents and the average value per patent. In addition, the elasticity of value with respect to portfolio size is sizable shows that value rises proportionally or even more because the average quality does not decline (Gambardella, et al., 2017).

After having discussed a wide range of literature on how to measure the economic value of patents, using few methods and theories, we will now focus our attention on the Pharmaceutical Industry in Europe and India, and their Patent System.

CHAPTER TWO: PHARMACEUTICAL PATENTS

2.1 How TRIPS affects pharmaceutical patents

During this Coronavirus pandemic, the global scientific community is demonstrating an incredible willingness to share knowledge of potential treatments, coordinate clinical trials, develop alternative models and publish immediately all their findings. In this positive and collaborative climate, it is really easy to forget that commercial pharmaceutical companies, for many years, have been privatizing and locking up the knowledge commons (Stiglitz, et al., 2020), by extending control over life-saving drugs with the use of unnecessary patents, and by lobbying in opposition to the generic medicine industry.

As mentioned in Chapter One, a patent is a property right granted by the government of a country to the inventor of a novel, non-obvious and useful invention. When a patent is granted, the owner has the right to exclude other from making, using, selling her intellectual property for a period of 20 years. In return, the patent holder publicly discloses their invention: this facilitates free use of this information when the patent expires.

Patents work differently in different industries. In the electronics sector, patents are mostly shared among companies thanks to the pooling and/or cross-licensing of them. This is true for example for the modern smartphone industry, in which every hardware and software component has been patented by a different manufacturer. This sharing of technology is fundamental since a specific product contains many patented technologies. On the other hand, in the pharmaceutical, chemical, biotechnological industries, the patent most of the time is the product itself. Therefore, a patent is necessary to protect the effort put in the research and development, and clinical testing required before being able to place it in the market. Patent protection for the pharmaceutical products is particularly important compared to other sectors, since the manufacturing process is way easier to replicate by other competitors, with a fraction of the initial investment. The massive amount of investments needed to produce a new drug or vaccine means that the pharmaceutical companies redirect their effort in meeting the health needs of developed countries, where they can get profits. This is due to the fact that in those countries, patent laws are very flexible in issuing patent grants and the average wealth is high enough to allow most of the population to buy the medicines they need, or have a developed public health system in place (for example the vast majority of countries in Europe).

Before the TRIPS Agreement entered in force, in most countries there was no patent system in place, or even if there was, it had very strict rules when granting patents to inventors. For what concerns pharmaceutical ones, there existed countries where there was absolutely no patent

system whatsoever in place. Also, TRIPS allowed least developed countries to abstain from to complying with the Agreement until 2033. Some scholars believe that the lack of patent protection for pharmaceutical products in these countries makes it difficult to establish research-based industries in most of these places. For this reason, most medical research takes place in the public sector. The lack of any means of patenting suppresses the development of commercial enterprises focused on alleviating the disease burdens common to least developed countries. This is the approach followed, for instance, by Lehman (2003), who justify the existence of a flexible patent system as the main instrument to increase the capability of the pharmaceutical industries in developing countries, to produce drugs that can cure the local diseases at an acceptable cost. Also, efficient national patent laws better reward the effort of pharmaceutical companies which work for years to put in the market a safe drug. Therefore, the research and development of a firm, which is the most financial resource-consuming activity of a pharmaceutical company, is rewarded. While he admits that markets are morally neutral and work on the principal of scarcity, he states that in most cases the lack of access to the most innovative technologies is not a necessity (Lehman, 2003).

However, Lehman (2003) ignores that since patents eliminate competition, they can also lead to high prices for medicines during the term of the patent. High prices, as well as the need for particular drugs, defeat the goal of providing universal access to a list of essential medicines, especially in low-income countries. In addition, the incentive to invest in research and development in order to bring alternative medicines to market may not be present when the market value of the innovation is insignificant. In the case of "neglected diseases" that essentially affect poor populations and the least developed countries, patents have failed to achieve their objective as instruments of innovation since both governments and the people in need, lack the purchasing power to create a market that justifies the necessary investment in the first place. Other policy instruments are required to overcome market failure and to encourage research and development for neglected diseases, and to stimulate local industries (Magnusson, 2017).

Notwithstanding the two different views on patent, the TRIPS Agreement has some provisions in place that make it more flexible to support the needs of the developing countries.

For example, government may use or allow a competitor of a patent holder to use her invention without consent. This right of public power, commonly called "compulsory licensing", include protection of the patent owner by granting them royalties if an invention is used, or being able to negotiate with the patent holder. In any case, this rule does not apply in situations of national emergency, or in public use for non-commercial purposes. This tool has been established so that national governments can prevent any potential abuse by patent holders and put public

interest first, including protecting health by guaranteeing that people have access to essential medicines. The latter aspect was the primary reason of existence of the 2001 "Doha Declaration on the TRIPS Agreement and Public Health" mentioned in Chapter One. With the Declaration it was reaffirmed that "countries which does not have the capacity for domestic production of a needed product should be no less protected by compulsory license provisions (or indeed other TRIPS safeguards), nor should they face any greater procedural hurdles, compared to people who happen to live in countries capable of producing the product" (World Trade Organization, 2001). Therefore, this flexibility enables governments to improve access to patented medicines that the inventors could make it difficult to use, by supplying small quantities or imposing a higher than optimal price. Because TRIPS allow compulsory licensing mainly to supply the National market, selling medicines to other countries is a process that can be subject to restriction. Consequently, this system does not support countries that do not have in place an efficient pharmaceutical industry and are forced to rely on imports. The World Trade Organization, few years after the Doha Declaration, agreed terms that allow the issue of compulsory licenses specifically for export, for countries that are not subject to the TRIPS Agreement until 2033; but this process is very complex and has never been really exploited (Grillon, 2017). India, among others, tried to lobby against this process. Indeed, the country has always been considered the "pharmacy of the developed world", being the largest exporter of pharmaceutical products to the poorest countries, thanks to its affordable prices. In definitive, compulsory license is not enough to circumvent the strong patent system that TRIPS has imposed to all countries that are part of the WTO.

Furthermore, according to a TRIPS Agreement provision, World Trade Organization's members can also build a more balanced national patent system which takes into consideration both the patent holders and the public interests. Specifically, this concerns the definition of patentability, meaning how we specify the conditions that make an invention patentable. The Agreement states that governments can exclude specific inventions from patentability (World Trade Organization, 1994). As already mentioned, in order to obtain a patent, inventions must possess three key characteristics: they must be new, involve a creative step (i.e. non-obvious for a person specialized in that field) and be used for industrial application. TRIPS does not define clearly how those three main characteristics can be interpreted. Therefore, each country is free to state their interpretation of these conditions within their national laws. Going back to the Indian case, their patent law requires that novel forms of already existing medicines, have to satisfy an additional therapeutic benefit to "gain" the condition of the creative step. In this way, one of the major instruments that pharmaceutical companies exploit to obtain lifetime monopolies on their drugs, i.e. evergreening, becomes useless.

Countries that want to guarantee a rigorous application of the patentability conditions, must ensure a transparent process of investigating and granting patent rights, as well as for opposition. The latter allow all interested third parties (for example competitors or any other stakeholders) to give adequate reasons for rejecting any patent requests and for revoking already existing ones. Regrettably, most countries have not enforced this kind of procedures efficiently enough (Grillon, 2017).

If certain conditions are met, TRIPS allow governments to provide limited exceptions to patent rights, for example permitting the use of a patented invention in research and academic studies on expiry of the patent. It also restricts the "power" of patents by granting countries the possibility to resort to parallel imports, which is the purchase of a product protected by a patent on a market other than the national one where it could be cheaper.

Last but not least, a transitional period has been granted to poor countries classified by the UN as Least Developed Countries (LDCs), during which they are not required to meet TRIPS obligations, continuing to be part of the WTO. With regards to the pharmaceutical industry, the period will end the 1st of January 2033. This exemption has not been applicable to all LDCs, because some African countries, part of the ARIPO (African Regional Intellectual Property Organization) have established stronger patent system than TRIPS (Grillon, 2017).

Nonetheless, what is happening in practice is that the implementation of TRIPS flexibilities to improve access to essential medicines is being hampered by the economic and political pressures of pharmaceutical companies, and by some developed countries such as the United States, Switzerland and the European Union. One recent example is the effort by both the US and Swiss governments to discourage Colombia from the compulsory licensing of imatinib, an anti-cancer drug. Countries that use mandatory licensing have had a significant price reduction and an increase in production of generic drugs, hence improving access to life-saving HIV therapies (such as Thailand and Brazil), or certain cancers (India). The ability of the countries to effectively uses the flexibilities depends on the economic power and the ability to withstand external pressures. The European Union is a powerful example of the political imbalance against the use of TRIPS flexibilities. Also, the United States and Japan have imposed stronger standards for protecting intellectual property (TRIPS+).

In any case, the efficient use of TRIPS flexibilities is the main course of action to reach an equilibrium where the public health and the private interests coincide, or, at least, do not interfere with each other. Unfortunately, these instruments have not stopped most pharmaceutical companies to use mechanisms to circumvent the rules and get lifetime monopolies on their inventions.

2.2 Market manipulation

A company willing to bring a new drug in the market must first of all develop the drug, determine how to produce it in large quantities consistently and prove to the national drug agencies that the product is safe and effective, after the conduction of rigid and appropriate clinical trials. Those inventions that meet all the above characteristics "win" the lottery and obtain the right to exclude others from making, using or selling the drug. Since inventors try to patent their chemical compounds early in the development cycle, some of the patent terms will expire way before the drug gets into the market. This is because clinical trials and all the studies needed to guarantee the safety and efficacy of a drug are processes that can last a decade.

According to Feldman (2018), the average residual patent period for a new drug is 12 years, which is almost half the 20 years established by TRIPS but is a considerable reward, nonetheless. When the patent expires, a normal patent system allows generic companies to step into the market using that specific patent (or patent portfolio).

Often, the generic company needs only to demonstrate bioequivalence, a term indicating that it does not have to show that the chemical formula is safe and effective, but just that the product is identical as the patented brand. In this way a company can enter the market without incurring the huge research and development costs needed for the first approval of the drug, hence being able to price the generic medicine at a much lower cost than the branded one. In addition, generic companies do not rely to advertising, but they depend on drug substation laws that allow family doctors or pharmacists to prescribe the generic and cheaper version of a brand drug (Feldman, 2018).

The introduction of generics is a socially positive shock to the pharmaceutical industry. When the first generic enters the market the price drop is almost 20% of the monopoly price while with multiple generics, the prices may suffer a larger drop in the order of 80–85% (FDA, 2018). These issues force drug companies into trying to delay competition for as long as possible. To that purpose, they do all they can, starting from price increases on the drugs that are still patented, or to use the infamous "evergreening" mechanism.

Evergreening is a corporate strategy that is achieved by seeking extra patents on (often small) variations of the original drug that can be new forms of release, new dosages, new combinations or variations, or alternative forms. In the pharmaceutical industry, this is referred to as "life-cycle management". Even if the patent is not so innovative, the company can earn more from the higher prices than it pays in legal fees to keep the patent alive (The Conversation, 2014).

Kapczynski et al. (2012) study on secondary pharmaceutical patents granted between 1985 and 2005 by the FDA shows numerical result on the "evergreening" mechanism. They call them "secondary patents" not because they believe that these patents are of lesser importance of

strength, but because they are assumed to come later in the sequence of innovation, and to offer less robust protection than a primary chemical compound claim. First, they show that patents with secondary claims are very common. Then, they find that independent secondary patents on average increase the duration of the nominal patent term enjoyed by drugs. When the secondary patents are on chemical and pharmaceutical compounds, they add on average between 4 to 5 years of additional nominal patent term. Patents that do not rely on pharmaceutical compounds hugely depend on secondary patents: here they add more or less 10 years to the standard period (Kapczynski, et al., 2012). In addition, they demonstrate that independent secondary patents are not randomly distributed. Indeed, the propensity of firms to request secondary patents after their drug is on the market, increases over the sales distribution, showing that companies deliberately attempt to lengthen their monopoly.

Other evergreening strategies involve the development of new chemical formulations, dosage schedules, or combinations that allow companies to request new patents (Feldman, 2018). In addition to the previous strategies, companies advertise extensively to move the market to the "new" product, pressuring doctors to write the new medicines or ultimately removing the old drug from the market. These procedures, of course, do not allow pharmaceutical firms to continue enjoying the patents' benefits but somehow are forms of market manipulation, so they will still continue having buyers that do not shift to the generic versions.

The most notorious evergreening technique is applying for new patents. There are very few patent law systems in the World that really challenge the actual validity of the patents, and litigation is an expensive and lengthy process for a generic company to go through. Companies that are able to obtain new patents on slightly modified inventions, minimize not only the damage they would have incurred if they were pushed out from their monopoly, but they can even eradicate the issue of being on the edge at all.

In definitive, even though it is safe to assume that competitors will enter the market after a pharmaceutical patent expires, in reality this rarely happens at all. A significant number of strategies and possibilities exist, so that companies can exploit them to extend their protection and increase, indefinitely, the period of market monopoly for their drugs.

Feldman (2018) demonstrate, using US patents data from 2005 to 2015, that the pharmaceutical industry has strayed far from how the patent systems' have been designed by the legislators. First, he finds that almost 80% of the drugs associated with new patents in the FDA's records, were not new-coming drugs on the market, but instead already existing ones. Second, among the 100-best-selling drug in the US, over 70% extended their protection one time, and 50% more than once. Last, almost 40% of all drugs present in the market created additional entrance barrier to continue enjoying the monopoly (Feldman, 2018).

2.3 The GLIVEC case

On the 1st April 2013, the Indian Supreme Court delivered a verdict that affected the national and global conversation about patents. They denied the request from one of the biggest and powerful pharmaceutical companies, the swiss Novartis, to grant a patent on a slightly modified form of an important cancer curing drug, Glivec. The verdict of the Supreme Court determined a historical win for the access to medicines movement for patients in lower income countries. For the first time in history, the universal health right of the population has been put at the first place, protecting at the same time the local pharmaceutical industry that is specialized in the production of generic drugs. Indeed, India is the biggest exporter of generic products to the poorest countries in the world, who in this way can afford medicines that otherwise would be inaccessible to them because of the high prices that big pharmaceutical companies impose on patent-protected drugs.

In Italy, in 2017, the price of a box of 120 Glivec pills was 1.800 Euro, valid for a month of treatment. Hence, the yearly cost for a patient was almost 22.000 Euro (Arletti & Bocci, 2017). The generic version of the same drug, instead, costed at the time 50 Euro a month.

Given the ability of India to produce large quantities of safely produced medicines at affordable prices, India is known as the "Pharmacy of the Developing World", since it has become the biggest supplier of generic drugs in many poor countries (Médecins Sans Frontières, 2005). Thanks to India's generic industry, the standard treatment for AIDS, the so called "triple therapy", that costed patients in the developed countries a staggering amount of 20.000 USD per year, was made available at less than 200 USD per year few years ago.

Since 2005, all developed or developing countries part of the WTO, like India, has been obliged pursuant of the TRIPS Agreement, to establish an efficient patent law system in line with global standards. India, with its Patent Act of 1970, has been one of the few countries in the world, in where to get a patent you had to follow a rigorous procedure. Consequently, this has presented the country a numerous amount of legal cases that challenged the position of India as the pharmacy of the third world.

Novartis was among the companies that appealed to the Supreme Court to obtain a patent on a modified version of its cancer drug, Glivec. Studies have shown that Glivec (or better, the chemical compound from which it derives) is the most effective existent interferon therapy (Lee, 2008) but it does not cure cancer permanently since it only stalls its progress. This means that a patient has to take the drugs during her lifetime. As almost 70% of the Indian population lives on less than 2 USD per day (Lee, 2008), the pricing of medicines, especially the life-saving ones are crucial. The difference in prices between the generic and the brand drug is quite impressing, as previously mentioned. For this reason, in 2006, the Indian Patent Office rejected

Novartis' patent application for Glivec under Section 3(d) of the Indian Patents Act, pointing out that the company was trying to use the "evergreening" strategy to extend its monopoly on the drug (to patent or not to patent).

Gabble and Kohler (2014), reviewed the history of the attempts of Novartis to file patents in India for Glivec. They found that in 1993, Novartis filed patents worldwide for the imatinib pharmaceutical compound (that they later called Glivec) but they could not request it in India, as the country did not grant patents to products at the time. Novartis tried again in 1997 when they completed the product and made it marketable, and India accepted the patent application under the "mailbox" provisions, a scheme which allowed companies to request patents in India while the country was transitioning to the TRIPS Agreement system. During that period, Indian generics companies were producing the same version of the drug at a tenth of its original cost, so this market pressure forced Novartis to turn to the Indian Government and request a stand on the matter. The Indian Government therefore granted the company exclusive selling rights while their application came up for review. This decision blocked the generic industry that was producing the medicine, and resulted in a protest, led by the non-profit Cancer Patients Aid Association (CPAA) and the subsequent filing of opposition against the company's patent application. In 2006 the Indian Patent Office finally rejected the patent, citing that it did not demonstrate any significant changes with respect to its previous form, which were already patented outside India (Gabble & Kohler, 2014). Novartis attempted several times to overturn the decision of the Supreme Court and the Section 3(d) of the Indian Patents Act. The final decision, in 2013, confirmed the previous stands against the grant of the patent to Novartis, putting the protection of the public health as the primary reason for the reject.

According to Novartis, the requirement under Section 3(d) of the Indian Patents Act which introduced "a new efficacy enhancement hurdle" (Novartis, 2009) for patenting new forms of known compounds, should not have been applicable to Glivec, since it has "changed the lives of patients with rare cancers" being "one of the major medical breakthroughs of the 20th century". In their opinion, the patent they requested was necessary because the previous chemical compound was only the first step in the process to develop Glivec as a viable treatment for cancer. They justified their request stating that the R&D, which took years, created more than just an incremental improvement. The outcome of the Glivec case would not have hindered the supply of essential medicines, they pointed out, since international trade rules include safeguards to ensure patient access. Novartis stated that they recognized the contribution of generics to improving public health once drug patents expire, but also that many patients need further help to gain access to the medicines they need. The company designed few programs to help under-developed countries to afford their medicines, especially in India. Finally, Novartis

issued a rather colorful statement according to which the result of the Glivec case would have set an industry precedent as to whether pharmaceutical companies would have been able to invest in R&D in innovative medicines for India and will have determined whether or not innovation will be fostered considering India's intellectual property laws. India's effort to safeguard public health interests by denying Novartis the patent would have comprised the system that helps to create new lifesaving medicines for the people in need.

From the Indian Government point of view, Glivec should have been rejected because the modified version of the drug did not represent a significant change in effectiveness with respect to its previous version. India's Section 3(d) ban the evergreening practice in order to protect access to medicines for its population. Also, the programs created by Novartis to grant discounts to people in lower-income countries were still insufficient since the generic versions were still way more affordable. In addition, the 2001 Doha Declaration justified the reject of the patent since "the TRIPS Agreement can and should be interpreted and implemented in a manner supportive of WTO Members' rights to protect public health and, in particular, to promote access to medicines for all" (World Trade Organization, 2001). Therefore, the appeal brought by Novartis were actually not valid from the beginning, since Indian patent laws are indeed constitutional and TRIPS complying, contrary to the company's claims.

The final decision of the Supreme Court, that made the new Glivec molecule definitively not patentable, agreed with the Government stands. The verdict confirmed the right of India's Parliament to implement the measures that were included in the TRIPS Agreement with regards to public health safeguards. Furthermore, the decision repositioned India as one of the biggest producers of affordable medicines and reaffirmed its continuity as the "Pharmacy of the third world". Also, the outcome has functioned as a model to other developing countries, directly affecting for example Argentina and The Philippines, that adopted similar provision as the one contained in the Section 3(d) of the Indian patents laws (Chatterjee, 2013). Médecins Sans Frontières commented that the decision was a tremendous relief for millions of patents and doctors in poor countries who depend on affordable medicines from India, and for treatment providers such as MSF. The International president of MSF at the time, Dr. Unni Karunakara, stated that "The [Indian] Supreme Court's decision now makes patents on the medicines that we desperately need less likely. This marks the strongest possible signal to Novartis and other multinational pharmaceutical companies that they should stop seeking to attack the Indian patent law"[7].

[7] Full interview available at: https://www.msf.org/indian-supreme-court-delivers-verdict-novartis-case

The Glivec case is an important precedent for the fight on access to medicines, by putting the public right above the interests of a powerful pharmaceutical company, while at the same time following the laws.

2.4 Pharmaceutical industry and patent laws: Europe vs India

The principal objective of this thesis is to determine whether the Indian Patent system can set an example, a better one, for other countries, in particular the developed ones, with regard to access to medicines. We want to understand whether it is fair that pharmaceutical companies exploit more "passive" Patent Laws, such as those present in Europe, to get lifetime monopoly on their drugs. We also want to assess the Indian Patent system to determine its applicability on European laws, specifically regarding the Section 3(d) mentioned beforehand. Ultimately, we would like to verify if the main justification that companies make about the high prices applied for patented medicines, i.e. high prices are proportional to high R&D costs, are actually verified empirically. Of course, we know that obtaining Research and Development data, in the chemical and pharmaceutical area, is very difficult because of the high sensibility of the data. Therefore, a lot of the work will involve using unique sources for the data gathering. To answer the above questions, we will begin by comparing the pharmaceutical industry in Europe with the one in India, and then studying the patent laws of the two sides.

2.4.1 Pharmaceutical industry in Europe

The following table is re-elaborated from EFPIA[8] (2020), indicating the key data on the European Pharmaceutical industry during the last 20 years.

Table 1: Pharmaceutical industry in Europe. Values in millions of Euro unless otherwise indicated (source: EFPIA)

INDUSTRY	2000	2010	2018
Production	127,504	199,730	259,857
Exports	90,935	276,357	435,300
Imports	68,841	204,824	313,269
Trade balance	22,094	71,533	122,031
R&D expenditure	17,849	27,920	36,312
N° of employed	554,186	670,088	793,111
N° of employed in R&D	88,397	116,253	115,792

[8] The European Federation of Pharmaceutical Industries and Associations (EFPIA) represents the biopharmaceutical industry operating in Europe. Currently it represents 36 National Associations and 39 leading pharmaceutical companies, and an important number of small and medium-sized enterprises.

In 2018, in Europe the costs in research and development were about 36 billion of euros and the total number of employed in the sector was 793 thousand people. Nevertheless, according to the EFPIA (2020) report, the sector has been hit, besides the additional regulatory hurdles and increasing R&D costs, also by the impact of fiscal austerity measures imposed by European governments since 2008. During the period 2014-2019, the main emerging markets, i.e. Brazil, China and India, grew respectively by 11.2%, 6.9% and 11.1%, while the top five European markets (Italy, Germany, France, Spain and United Kingdom), in conjunction, grew only by 5%.

The following table, instead, depicts each European country's spending in R&D in 2018.

Table 2: European countries' spending in R&D in 2018. Data in millions of Euros (source: EFPIA)

Austria	278	**Latvia**	n.a.
Belgium	3,570	**Lithuania**	n.a.
Bulgaria	91	**Malta**	n.a.
Croatia	40	**Netherlands**	642
Cyprus	85	**Norway**	126
Czech Republic	36	**Poland**	356
Denmark	1,629	**Portugal**	116
Estonia	n.a.	**Romania**	80
Finland	216	**Russia**	944
France	4,451	**Slovakia**	n.a.
Germany	7,815	**Slovenia**	180
Greece	51	**Spain**	1,147
Hungary	242	**Sweden**	1,104
Iceland	n.a.	**Switzerland**	6,010
Ireland	305	**Turkey**	103
Italy	1,650	**United Kingdom**	5,045
TOTAL			**36,312**

Unsurprisingly, the countries that spend most in Europe are the ones that have the biggest GDP, being Germany, United Kingdom and France. Also, as expected, Switzerland, being home of few of the largest pharmaceutical super-powers of the world, has the second largest spending in Europe after Germany. The exception among the data is represented by Belgium.

Putting in perspective the previous data, during the last ten years in the US the growth in R&D expenditures has always been higher compared to Europe. In addition, Europe is facing

increasing competition from emerging and rapidly growing economies, so the geographical balance of the pharmaceutical market, and consequently the R&D, will probably shift towards those countries (EFPIA, 2020).

Notwithstanding, the spending in R&D actually does not reflect the actual production of pharmaceuticals in Europe, as shown in the following table showing the production of each country in 2018.

Table 3: European countries' production of drugs in 2018. Data in millions of Euros (source: EFPIA)

Austria	2,775	**Latvia**	157
Belgium	13,312	**Lithuania**	n.a.
Bulgaria	131	**Malta**	n.a.
Croatia	588	**Netherlands**	6,180
Cyprus	180	**Norway**	1,072
Czech Republic	858	**Poland**	2,456
Denmark	14,391	**Portugal**	1,514
Estonia	n.a.	**Romania**	655
Finland	1,773	**Russia**	4,537
France	23,213	**Slovakia**	356
Germany	32,905	**Slovenia**	2,010
Greece	996	**Spain**	14,970
Hungary	3,284	**Sweden**	8,153
Iceland	89	**Switzerland**	45,885
Ireland	19,305	**Turkey**	2,874
Italy	32,200	**United Kingdom**	23,039
TOTAL			**259,857**

Comparing table 2, with table 3, it seems that there are countries, such as Italy, that even if they do not spend a huge amount of resources in research and development, they obtain revenue on the selling of medicines for almost 30 times than the costs they incurred in R&D. Noting this peculiarity, it is interesting to find out the R&D to the sales ratio for all countries, as shown by the following table.

Table 4: R&D to total sales ratio for European countries in 2018. (source: elaborated from EFPIA)

Austria	10.02%	**Latvia**	n.a.
Belgium	26,82%	**Lithuania**	n.a.
Bulgaria	69,47%	**Malta**	n.a.

Croatia	6,80%	**Netherlands**	10,39%
Cyprus	47,22%	**Norway**	11,75%
Czech Republic	4,20%	**Poland**	14,50%
Denmark	11,32%	**Portugal**	7,66%
Estonia	n.a.	**Romania**	12,21%
Finland	12,18%	**Russia**	20,81%
France	19,17%	**Slovakia**	n.a.
Germany	23,75%	**Slovenia**	8,96%
Greece	5,12%	**Spain**	7,66%
Hungary	7,37%	**Sweden**	13,54%
Iceland	n.a.	**Switzerland**	13,10%
Ireland	1,58%	**Turkey**	3,58%
Italy	5,12%	**United Kingdom**	21,90%

Interestingly, Bulgaria and Cyprus, two of the smallest economies in Europe, spend respectively 70% and 47% in R&D with respect to their pharmaceutical production. On the other hand, more powerful economies, such as Italy and Ireland, have a very low spending in research and development. It is also worth noting that Switzerland, being one of the leading countries in the research area, is more than able to make up its costs.

Moving on the generics data, the following figure indicates the share accounted for by generics in pharmaceutical market sales (at ex-factory prices).

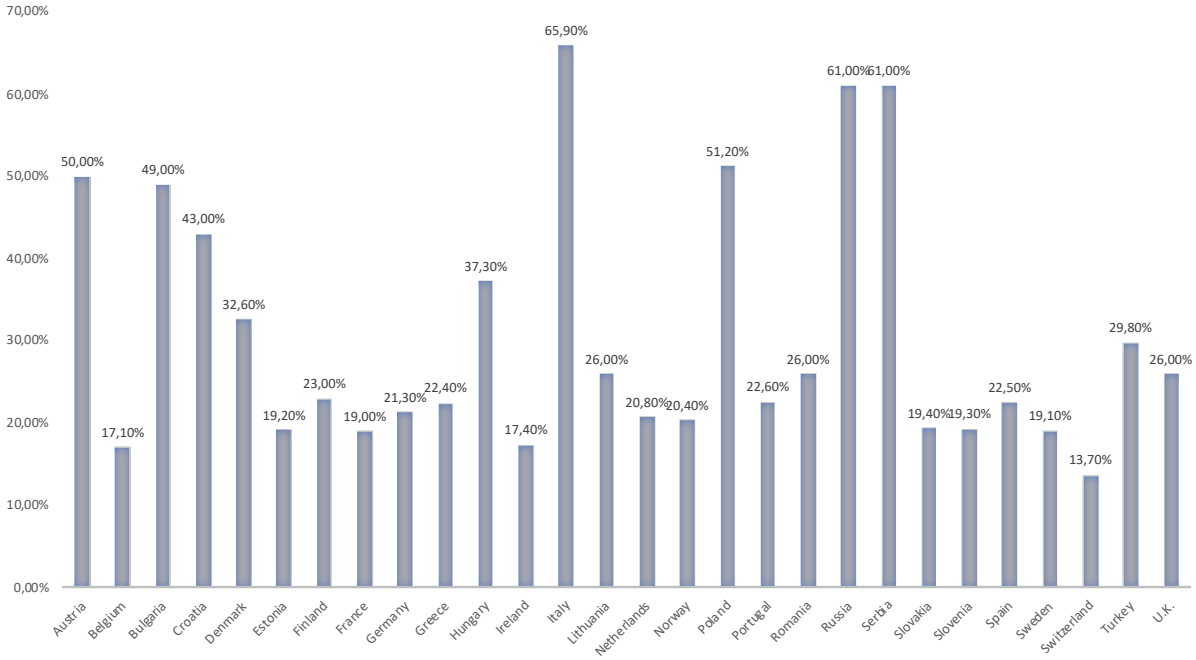

Figure 4: Generics sales to total sales ratio in Europe in 2018 (source: elaborated from EFPIA)

There are only 5 countries that sell over 50% of their production in the generic market, with Italy being the biggest one. Surprisingly, the second largest producer of medicines in Europe, Switzerland, sells only 13% of their total production in the generic market.

Last but not least, it is interesting analyzing the trade balance on pharmaceuticals. The following table shows the difference between the exports and the imports of all countries part of EFPIA.

Table 5: Trade balance of pharmaceutical drugs in Europe in 2018. Data in millions of Euros (source: Eurostat COMEXT)

Austria	327	**Lithuania**	-288
Belgium	6,632	**Luxembourg**	-207
Bulgaria	-451	**Malta**	43
Croatia	-242	**Netherlands**	13,374
Cyprus	48	**Norway**	-1,232
Czech Republic	-1,905	**Poland**	-3,295
Denmark	9,469	**Portugal**	-1,656
Estonia	-402	**Romania**	-2,297
Finland	-1,233	**Russia**	-9,854
France	4,619	**Slovakia**	-1,325
Germany	33,211	**Slovenia**	1,359
Greece	-1,734	**Spain**	-3,610
Hungary	847	**Sweden**	4,017
Ireland	34,236	**Switzerland**	47,027
Italy	-657	**Turkey**	-3,007
Latvia	-151	**United Kingdom**	368

It is no surprise that Germany and Switzerland have a very high positive trade balance. Instead, countries that do not have a relevant pharmaceutical industry are more dependent on exports, and therefore present negative trade balances.

In definitive, the industry in Europe is quite diversified, and very much dependent on the specific country part of EFPIA. It is interesting that there are small economies, such the Bulgarian one, that invests a lot in R&D if compared to their total sales. Furthermore, the generic industry is not quite developed in Europe, with few exceptions from Italy, which generics sales represent over 60% of its market. Finally, a country like Switzerland, a leader in the pharmaceutical sector, is one of the biggest spenders in R&D but is more than able to make up its spending.

2.4.2 Pharmaceutical industry in India

The Indian pharmaceuticals market has unique characteristics according to the McKinsey (2020) report on India Pharma. First, the generics dominate, making up for 75% of the retail market. Then, local companies have enjoyed a primary position driven mainly by early investments in the sector and production capabilities. Second, the high competition lowers the prices. The Indian industry ranks tenth in terms of value, globally, however it is ranked third in volumes. These characteristics present both opportunities and challenges (McKinsey, 2020).

Also, India is still the largest provider of generic drugs in the world, as it provides over 50% of the global demand for various vaccines, 40% of generic demand in the US and 25% of all medicine demand in the UK (IBEF, 2020). Currently, over 80% of the antiretroviral drugs used to combat HIV are coming from Indian pharmaceutical firms. In addition, Indian generics account for 20% of the global export in terms of selling volume.

In the last 5 years (2015-2019) the market size grew by almost 5 billion, as shown in the figure below, with an average yearly growth rate of 7.73%.

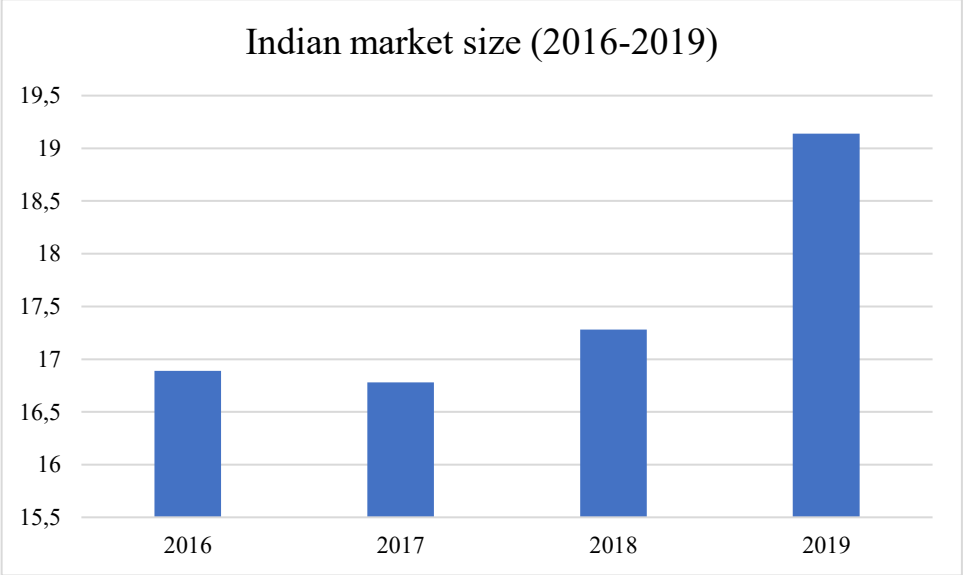

Figure 5: Market size in India in the last 5 years, in millions of USD (source: IBEF)

The exports industry also grew up during the same period, however not following a similar pattern in terms of growth rate, as suggested by the following figure which shows a small reduction of exports from 2016 to 2017.

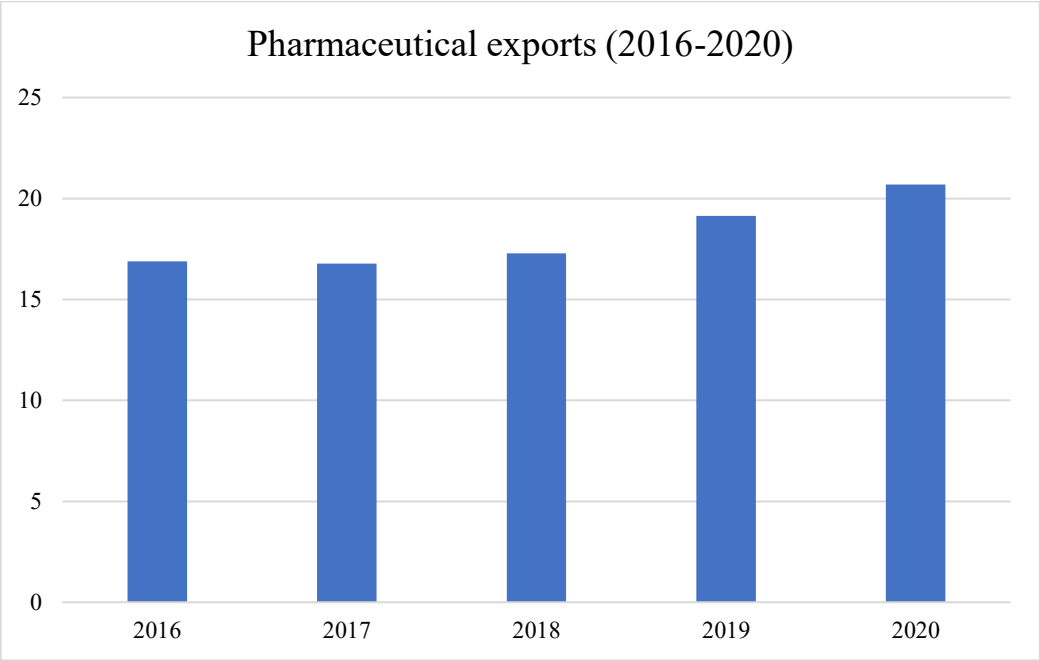

Figure 6: Pharmaceutical exports in the last 5 years, in millions of USD (source: IBEF)

The generic industry, as mentioned beforehand, is the most relevant component of the entire Indian pharmaceutical industry. Many experts throughout the world questioned the role of India as the "Pharmacy of the third world" trying to understand whether Indian generics were as effective as those manufactured in the US or in Europe. The Telegraph (2020) interviewed Dr. Arindam Basu, professor of epidemiology at the University of Canterbury in New Zealand who believes that, as all medicines are expected to go through the process of quality control and evaluation by drug regulators, such as the FDA, it seems reasonable to expect that generic drugs produced in India have the same efficacy of the American and European counterparts.

Currently, according to a report from Global Business (2020), the generic landscape is rapidly changing, being affected by cost pressures in the domestic environment, pricing pressures in developed markets (Europe and USA), as well as pricing hurdles introduced in India. Finally, regulatory authorities are demanding stricter compliance, increasing also the costs for the approvals needed to put the drugs in the market.

Having understood the difference between the European and Indian pharmaceutical products markets, we will now study the patent systems that are currently in place in those areas.

2.4.3 European Patent System

The current European Patent System (EPS) has consisted of National Offices (NPOs) and the European Patent Office (EPO) since 1978. The rules governing the system have changed administratively, legally and judicially in the last 40 years.

The EPO is the crucial point of reference for patent applicants, as it offers a service of one-stop-shop for the process of obtaining a patent (Graevenitz & Garanasvili, 2018). Once an applicant

gets the patent through the EPO, they must then validate (which is a much faster procedure with respect to the applying) the patent with each National systems (NPOs) in which they want the patent to take effect. As an alternative, firms can submit their applications directly to each National system. In any case, submitting an application to the European Patent System is more efficient because a patent granted by the EPO is much more likely to be successfully validated by the NPOs. Indeed, the primary advantage that companies exploit thanks to the EPO is a reduction of costs when getting a granted patent (Graevenitz & Garanasvili, 2018). On the other hand, using this procedure means carrying the risk of a rejection by the EPO. It could happen that EPO may reject an application while one or more NPOs would not.

In practice, Graevenitz and Garanasvili (2018) find that applicants request the patent to one NPO, and then apply to the EPO, to mitigate the risk of reject by the patent offices. The following table shows the number of applications and the patents that were actually granted by the EPO during the last ten years. It appears that the number of applications has been consistent during the period in the exam, but the number of granted patents has increased more or less every year, with an increase of over a thousand of granted patents from 2010 to 2019. However, it is interesting to note that the difference between the number of applications in 2010 and 2019 was actually much lower than the difference between the granted patents in those years.

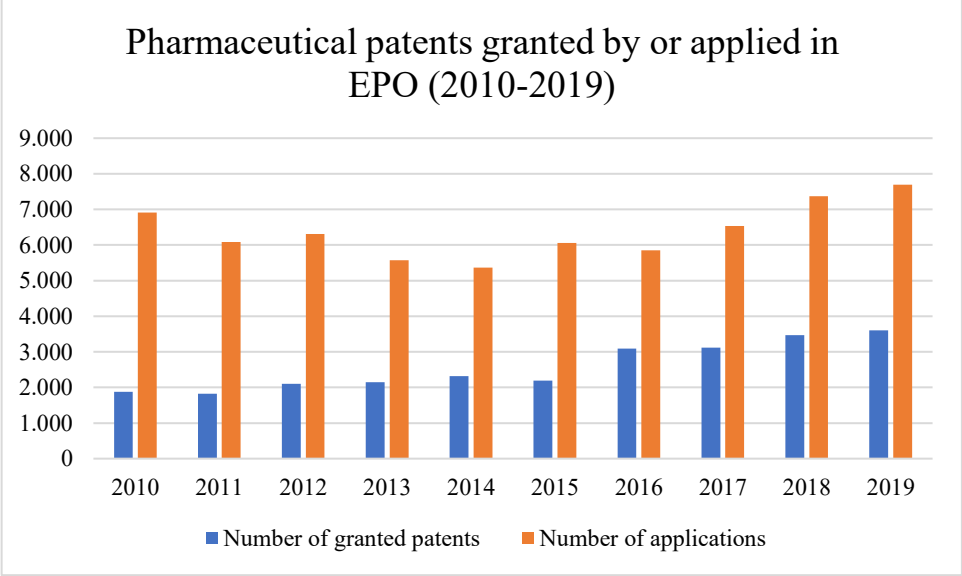

Figure 7: Pharmaceutical patents applications vs granted patents by EPO in 2010-2019 (source: adapted from EPO database)

The patenting process in Europe requires that the patent must possess the three characteristics already established by the TRIPS Agreement. For the EPO, an invention is patentable only if it is: new and previously undisclosed; distinguished by an inventive step not obvious to someone expert in that technology; capable of industrial application. Nevertheless, there are a few peculiarities in the EPO, for example, a computer software can only be protected by copyright but not by a patent, differently from countries such as USA or Japan.

There are 8 stages in the process for obtaining a successfully granted patent through the European Patent Office (EPO, 2011). First of all, the applicant must contact a patent attorney who will be able to provide more efficiently the documentation to the EPO. The documentation includes the formally written request, the details of the applicant, the description of the invention, etc. If the documentation is correct, the application is given a filing date (also called priority date). After this date, an initial examination begins. Next, a search report is sent to the applicant, listing and including copies of all prior art documents found by an experienced examiner and relevant to the invention in exam. The patent application is officially published after 18 months from the filing date. This means that the invention will be accessible to other people since it will be published in an open database. It will act as prior art against any future patent applications from other inventors or companies for similar inventions. The applicant has then 6 further months to decide whether to continue the application and if so, the countries which she wants to include in the patent protection. Accepting the continuation of the process means also being subject to the so called "substantive examination", which represents the next stage. Here the EPO has to decide if the invention and the application both meet the requirements of the European Patent Convention[9]. This is the crucial stage where the patent is evaluated by three EPO examiners for maximum objectivity, who interact directly with the patent attorney to discuss the feasibility of the patent and to discuss changes in the application. The sixth stage is the decision to grant the patent, after the approval of the examiners and the payment of all the fees. If it is granted, the patent officially takes effect from the date of publication. Following the grant by the EPO, the applicant has to validate the patent in each designated state within a specific time limit.

The patent may be opposed by third parties, if they think that the patent should not have been granted. The opposition can be filed during the 9 months following the publication of the patent in the European Patent Bulletin. This opposition stage is the ultimate resource of an opponent (usually a competitor) to attack a European patent as a single entity in a single forum. Indeed, after that period, the patent can only be challenged in national courts which ruling of course are independent of each other.

Currently, according to the EPO[10], it costs on average 6,100 Euro to take a patent application through the grant stage. This, of course, does not include the fees that an applicant may have to

[9] The European Patent Convention (EPC), dated 5 October 1973, is a multilateral treaty instituting the EPO and providing and autonomous legal system according to which European patents are granted. This convention basically represents the underlying framework to the current European patent system and includes not only the countries part of the European Union, but all European Countries, excluding Finland, Belarus, Ukraine and Russia, for a total of 38 countries.

10 Price source: https://www.epo.org/service-support/faq/own-file.html#faq-199

pay in addition, in some countries that requires a "complete" validation of the patent which requires a refiling of the patent and also the translation of the whole patent documentation.

The fundamental characteristic of the current patent system is that it enables inventor to get broad and uniform territorial protection in the participating Member States, with substantial costs reduction. A company that wants to patent its invention in more than one country, it just has to validate the patent in those countries rather than having to file individual applications. A validation process is much faster than applying for a patent in every country, and of course the fees are also much lower.

On the other hand, many companies believe that the current system's requirements to validate the granted European patent in every country separately is a real disadvantage. In a Finnish survey from the Confederation of Finnish Industries (2014), few companies replied that the European Patent System makes little sense as a concept, if the patent needs to be validated in each country separately, having to pay the validation fees in each country. Another perceived weakness of the EPS is that the registration of changes of the ownership after the grant of the patent cannot be done centrally by the EPO but must be made in each country separately.

The weaknesses of the current patent system could be solved by the new Unitary Patent system that is expected to start at the beginning of 2022. From 2012 to 2014, there have been significant developments in the implementation of the so-called "EU Patent Package" (Regulation No. 1257/2012) and the Agreement on the Unified Patent Court.

The Unitary Patent package will sit alongside the system currently in place and will provide a single pan-European patent and a single court for litigation of European patents (Roberts & Venner, 2014). The process of applying for a European patent, the examination of the patent application by the EPO, and the EPO granting process will remain unchanged under the new regime. The substantial difference is that it will be possible to get patent protection in up to 25 EU Member States by submitting a single request to the EPO. After a patent is granted, the patent holder will be able to request unitary effect, thereby getting a Unitary Patent which will provide uniform patent protection in up to 25 EU Member States (EPO, 2020).

Today, an inventor can protect an invention via a national patent or a European patent, however each granted patent must be validated and maintained individually in each country where they take effect. This is a complex and very costly process, as already mentioned, so the Unitary Patents will remove these kinds of issues. For example, no additional fees will be due for filing and examination of the request for unitary effect or for registration a Unitary Patent.

With the official implementation of the Unitary System, it is uncertain whether it will be easier for pharmaceutical companies to make use of the evergreening strategies described before, but considering the simplification of the process, it is more likely to happen.

2.4.4 Indian Patent System

The current patent law in India is governed by the Patents Act that entered into force in 1970 and was later amended in 2003, with the Patent Rules, and in 2005 with the Amendment to the Patents Act. The former is regularly amended in consonance with the changing environment, most recent being in 2016.

The patentability criteria under the Act are the same as the European System, as also India is part of the WTO, so are subject to the TRIPS Agreement (that was officially implemented in 2005 in India). However, the Indian System has different interpretations for some of the criteria. Indeed, the System requires that the invention is new (novel) and useful (industrial applicability), but non-obviousness (inventive step) is much stricter, contrary to the practice of patent laws in the vast majorities of the developed countries. It is worth noting that this peculiarity is also the instrument that allows the opposition and the revocation of patents under the Act. Also, in India, chemical and pharmaceutical inventions were only given process patents, but in 2005, to become compliant to TRIPS, the Amendment reinstated product patents and made the reverse-engineering or copying of patented drugs without requisite licensing from the patent holder illegal. Even though TRIPS forced India to transform its existing patent laws with the Doha Declaration, the country reserved the right to invoke compulsory licensing to fight the abuse of patent privileges. Most importantly, India inserted Section 3(d) into its amended law that made the patenting process a bit more difficult, particularly with regard to incremental innovation. Indeed, it is required that that an applicant has to demonstrate enhanced efficacy to the previously known substance to be considered a new invention (Khanna & Singh, 2015). The Section was specifically intended to protect consumers from the pharmaceutical companies that extended the patents on their drugs to enjoy lifetime monopolies.

When Section 3(d) was introduced, it was both unprecedented and unique among the world's existing patent regimes and was welcomed with a lot of skepticism by the developed countries. Nonetheless, a significant number of scholars and legal experts, after conducting independent assessments of the Indian patents law, have found that Section 3(d) was indeed compliant with the TRIPS Agreement.

The crucial requirement of "enhanced efficacy" established by the Section 3(d), according to Khanna and Singh (2015), are to be interpreted as a refinement of the "inventive step" and "industrial applicability" rather than a separate requirement. Another critic moved toward the Section 3(d) is that setting such high standards to patent inventions, discourages innovation and more in general, research and development. Notwithstanding all the criticisms, in a report from the Indian Pharmaceutical alliance, it has been shown that a list of 86 drugs that entailed relatively small changes over already existing compounds, have been able to demonstrate

successfully enhanced efficacy over the previous formulation, therefore obtaining patents in India (Khanna & Singh, 2015). Even though the report refers to data up to 2010, it is evident that it is not impossible to show the requirement of Section 3(d).

The following table compares the number of pharmaceutical patent applications and the patents actually granted, for the period 2008-2017. The number of patents that have been granted, compared to the number of applications presented to the Indian Patent Office, has been much lower. It appears obvious how the Indian patent laws are actually very strict in approving patents, with an average ratio between approved and filed of only 17.9%, meaning that less than ¼ of pharmaceutical patents applications are being granted each year. Furthermore, in the last few years, while the number of applications has always been more or less constant, it appears that the number of approved patents is increasing. This trend has also been present in the European figures shown previously.

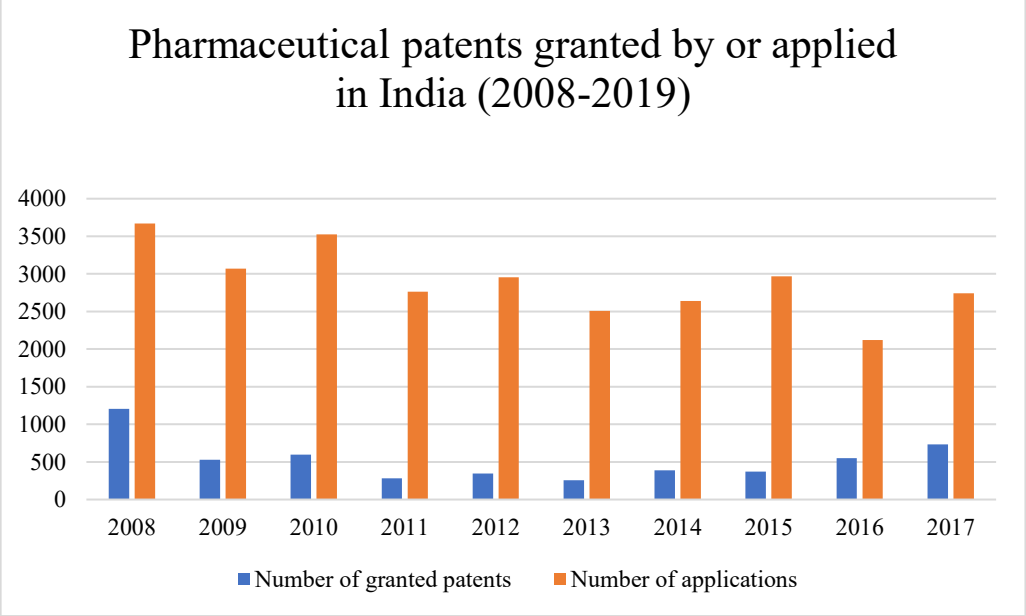

Figure 8: Pharmaceutical patents applications vs granted patents by IPO in 2008-2017 (source: adapted from IPO annual reports)

To get a patent approved in India, an applicant has to follow a predefined procedure, not very different from the one that is currently in force in Europe (with the EPO). Here, the starting point is to decide whether to apply for a patent personally or take help from registered agents (the latter is recommended) (IPTSE, 2019).

First, an inventor, or the delegated party, has to draft a patent application and needs to fill Indian Patent Application Form 1. The application should include clauses such as usability and outcome of the invention in details and any intention to license or profiting from the invention. After the first stage, the patentee can officially file the application, which needs to be submitted after the filling-out of several application forms. In the next stage the patent application is then

published in an official patent journal after a period of 18 months, unless the inventor does not submit a specific form, requesting an earlier publication. Before a patent is granted, it is scrutinized to determine its merits. This is not an automatic process since the applicant needs to request the examination formally, by submitting a form; then, the patent office queues the application for examination, with no fixed date. After the review of the application, a first examination report is completed by the examiner, indicating a detailed list of objections. Depending on the severity of the objections, the application process can delay of another 6-9 months (IPTSE, 2019). Once the examiner finds no objection whatsoever, the patent is granted and then published in the official gazette of the Indian Patent Office, with a protection period of 20 years from the date the patent was first filed.

One peculiarity of the Indian system is that the opposition process is rather effective, as it admits both pre-grant opposition and also post-grant opposition. The former can be filed by any party interested within six months from the date of the publication of the application in the official patent journal and not fees are required. For what concerns the post-grant opposition, it can be filed within twelve months from the date of publication of the grant of a patent in the official gazette of the patent office.

Without considering the annual fees that an inventor has to pay to renew the patent every year, the average cost for successfully getting the grant of a patent varies depending whether you are an individual, a small enterprise, or a large company. Considering as a baseline a small entity, the average cost if you apply for the grant directly and if you take help from experts, are respectively 160 Euros and 1160 Euros[11]. The costs can increase a lot if you are a large enterprise, with a maximum costs 2205 Euro, if you are both a large company and you subcontracted the filing of the application to a law firm.

The Indian patenting process, in conclusion, is rather complicated and involve almost 30 forms that you have to fill-out depending on the specific application and the needs of the applicant. In any case, even if the costs for patenting may seem much lower if compared to the European patents, the opportunity-costs are not so immediate. Indeed, in Europe you pay a higher fee, but the process itself is much more straightforward to complete. In addition, the process will become more efficient with the introduction of the Unitary Patent which will allow an inventor to request a patent in almost all countries in the European Union, with only one application. On the other side, requesting a patent in India, from the perspective of a foreign company, for example, a pharmaceutical company, is rather inexpensive, but the process itself is tribulated by the many technicalities of the Patents Act. Often, a pharmaceutical company is unable to get

[11] Prices source: https://www.zatalyst.com/cost-patent-registration-india/

a patent, even if it that had no problem getting it approved in other countries (the Glivec case discussed previously is a significant example in that aspect).

Having understood the differences in the European and Indian model, in the next chapter we will try to understand whether the Indian patent system can be an example for the European one. In particular it will be interesting to study if the Indian system can be applied to a more developed economy, and if the balance between public and private interest will be maintained. In addition, the main justification for the existence of patents is that they stimulate research because they protect inventions, allowing inventors to enjoy an established term of exclusive monopoly, to recover the costs of the research. However, is this true for pharmaceutical companies that strategically patent minor variations of already existing medicine, to maintain a monopoly in the market? We will try to focus our attention on the debate on research and development and patenting strategies.

CHAPTER THREE: R&D AND PATENTS

3.1 Innovation and access to medicines

Pharmaceutical companies' main justification on their continuous patent protection requests is the enormous amount of efforts and economic resources dedicated in developing the formulation needed to put a new or a modified drug in the market. In addition, the process of creation and marketing is of course long, costly and sometimes perilous. Therefore, patents, and other intellectual property protections, are thought to be an adequate reward that at the same time stimulates innovation and bring profits to companies. Notwithstanding, for pharmaceutical firms to have an incentive to continue investing in research and development, they must have an expectation that they can charge prices high enough to recover the R&D costs and still being able to make a profit. According to Grabowski et al. (2015) the main rationale for intellectual patent protection in the pharmaceutical industry, and generally for technology-driven industries, is that the long-term benefits that companies bring with continued future innovation outweigh the short-term monopoly that the protection results in.

DiMasi et al. (2016) find that the research and development processes often take over 10 years to complete and a new drug approval in the US involves more than a billion dollars in out-of-pocket costs. Furthermore, only one in eight drug candidates survives the approval process (DiMasi, et al., 2016). As a result, the high risk of failures, together with the vast amount of costs, mean that R&D expenditure must be funded by the new market-approved products. Without a patent system, it can be argued that the incentive to follow such a laborious process would disappear. Indeed, Mansfield (1986) found that, when there is no patent protection system, 60% of pharmaceutical inventions would not have been developed and 65% would not have been commercialized. Since the time of the study, efficient patent systems have been created all over the world, with TRIPS becoming a compulsory requirement to being part of the World Trade Organization. Consequently, it is rather safe to assume that the percentages found by Mansfield (1986) would be higher if the study was to be conducted now.

Finally, patents are also fundamental for start-up firms, often financed by venture capital. The value of these new companies is determined mainly by their proprietary technologies and the drug formulations they have under development. Hence, the existence of intellectual property protection plays a key role in funding and partnership opportunities for such firms (Grabowski, et al., 2015). Hsu and Ziedonis (2008) provide evidence that patenting positively affects investors' perceptions of start-up quality across multiple stages of the entrepreneurial life cycle.

Alongside this view on patents as an instrument that promotes and protects innovation, stands the access to medicines discussion, with the World Health Organization being the biggest voice. All the medical innovations, health technologies and novel drugs, have resulted in a drastic reduction of deaths, transforming many of the formerly deadly diseases to curable or at least manageable, also thanks to the intellectual property systems which have increased their importance over the last decades. Nevertheless, currently over one third of the world's population has no access to the benefits of the modern medicines and continues to die every day. While in the developed part of the world, many dangerous diseases and infections have disappeared, such as the infamous HIV/AIDS, in many countries all over the world this disease is still the main cause of death, for example in sub-Saharan Africa (Boschiero, 2017). There is also the resurgence of many other infectious diseases and a growing amount of incommunicable diseases, which kill, according to WHO, over 50 million people per year. For these typologies of diseases, there are no incentives for pharmaceutical companies to invest in research, as the country in which these diseases are mostly widespread, do not offer profiting opportunities, even with the existence of intellectual property protection. These problems explain why the patent system in the pharmaceutical industry is at the very center of the global discussion on the obstacles that do not allow easy access to medicines to all people, notwithstanding a person's wealth. For firms operating in the pharmaceutical and biotechnology field, the current way to finance and make available important innovations, is through the monopoly they enjoy after a patent is granted. The result of such market-driven and profit-oriented approach is that research in un-profitable diseases is simply not initiated by companies. At the moment, most R&D, are based on financial potential rather than the needs of the poorest and marginalized communities. Rare and neglected diseases that are affecting disproportionally small and poor proportions of populations, are not attractive enough to investors because of their low purchase power (Boschiero, 2017). Besides the non-existing research on particular areas, pharmaceutical firms exploit "evergreening" mechanisms to extend their monopoly indefinitely, requesting patents on small and very often pointless variations on the previous formulations (see Chapter Two), impeding access to medicines also with these legally allowed techniques.

Notwithstanding the two views on patents, it is fundamental answering the question on whether the patent system is really the most efficient way to go, or other alternatives exist that do not directly or indirectly endanger the life of the poor populations in the least developed countries in the world. Some critics of the intellectual property-based systems have stated that they could be replaced by prize systems or government contracting, options that may be better suited to balance the price competition and innovation incentives (Grabowski, et al., 2015). Indeed, direct government contracting could substitute private firms' research and development

spending, while a prize system could be applied to specified drug innovations. In both cases these incentives would be funded by taxes. This increase in taxes for people would mean that they could almost immediately benefit from prices reduction on all the medicines covered by these programs (Grabowski, et al., 2015). This means that people that have an immediate need for specific drugs, that would normally be protected by intellectual property and regulatory exclusivity, would now have a much easier access, especially considering the price reduction. On the other hand, direct government contracting would require an efficient gathering of information and decision making that could bring uncertainty to the pharmaceutical industry. Another linked issue would be the decision on picking the winners, in an industry that is always changing and developing (in particular if you also consider the biotechnology field). Considering how the current lobbying from Big Pharma affects the international market, many governments could be more lenient towards specific firms, without an impartial evaluation of the winner. However, when there is no market available for certain diseases, as before mentioned, government incentives could be useful to increase the research on those areas. Adequate and consistent investments by governments, in underdeveloped therapeutic fields and the public health connection between developed and less-developed countries is highlighted by the recent examples with diseases like Zika and Ebola.

The other alternative is the use of prizes, as they have the advantage of rewarding outputs instead of funding the research itself. This could reward other market participants, compared to the current industry. In any case, prize systems could be subject to several challenges, especially if they were to become patents substitute. According to Grabowski et al. (2015) prizes, most of the time, require clear and specified performance criteria, which it is likely to depend on one's interpretation. Also, as the research and development in the pharmaceutical industry is long and costly, the incentive to invest could be subject to hold-up issues. Therefore, inventors could simply decide that the incentive is not high enough to justify the risk that they are going to incur, as government prizes are connected to how the government is operating at the moment. Indeed, budget constraints and legislature changes could reduce the initially established prizes, or in any case cause destabilization to the market.

The debate on how to design a balanced intellectual property system that at the same time rewards the inventor and protects public health is destined to be crucial in the next years. On one side, patents' do represent a threat in poor populations. However, an efficient patent system with targeted R&D incentives to address unmet needs when market incentives are inadequate, alongside with policies encouraging price competition and the use of generics, is likely to remain the core approach for achieving these objectives.

Within this context, our aim in the next sections is to find how much different are the countries in terms of research expenditure, profitability and efficiency of R&D. In addition, we would like to find some relationships between the profitability of a country and its patenting strategies. More specifically, our ultimate objective is to understand if a model that has the characteristics of the Indian one could be applied to more advanced countries. First of all, we will start from analyzing research and development data from the main pharmaceutical companies all over the world, dividing them in geographical areas: Europe, USA, Japan, India and China. Second, we will focus on the comparison between Europe and India, trying to assess the efficiency of R&D with respect to the patent system. Finally, we will study whether the Indian patent system can be applied to the European countries and if there is one more suitable in terms of research stimulation and public health protection.

3.2 R&D costs in the world

Our data on research and development are based on the yearly R&D survey issued by the European Union, from 2013 to 2019. Looking for data on research and development is quite difficult because usually they are information that companies dislike disseminating, to maintain their inventions as secret as possible, especially if they represent a technological advance. In addition, it is impossible, with publicly available documentation, to understand what part of the R&D cost is devoted to which type of research. In definitive, this survey-based dataset is the only source of information that we have been able to gather together. Each yearly survey contains the first 2500 companies in terms of research and development expenditure in the world (but based in Europe), in all industries. Filtering by the pharmaceutical industry and trying to maintain consistency over the period in analysis, we have obtained data for 119 pharmaceutical companies from Europe, USA, Japan, India and China. We then extracted all firms' R&D costs, profit, and number of employees. With the word "consistency" we mean that we have taken into account only the firms that were present in the dataset during the entire period in analysis (i.e. 2013-2019). In addition, there were few specific data that were not available at all. For example, for the Indian company Cipla, the number of employees for the year 2015 was not present in the 2015 Survey. As our objective was to obtain a large dataset, instead of eliminating the company from our data, we applied the average growth rate for that parameter to find out the missing data.

Nevertheless, most of these companies are from the European, American and Japanese industries, while India and China account for 10 companies out of 119. Notwithstanding the differences between these areas, this is the most comprehensive dataset we have been able to retrieve from publicly available information.

We will start our analysis from a general overview on the total research and development costs during the period in analysis.

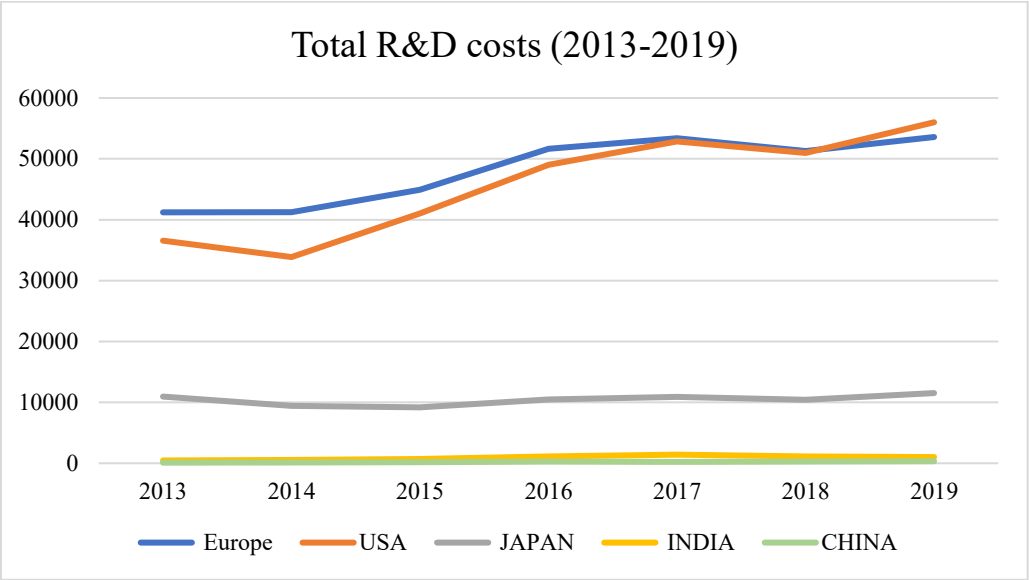

Figure 9: Total R&D costs during the period 2013-2019, in millions of Euros (source: own elaboration)

Unsurprisingly, the companies that spend more in research are from the USA and Europe, with the other countries really behind. Also, the total expenditure in Europe and in India are larger than USA and China, respectively. Nonetheless, it is worth to note that the figure is largely affected by the number of pharmaceutical firms for each group. The next figure may be more revealing, because instead of the total costs, shows the average costs for each geographical area.

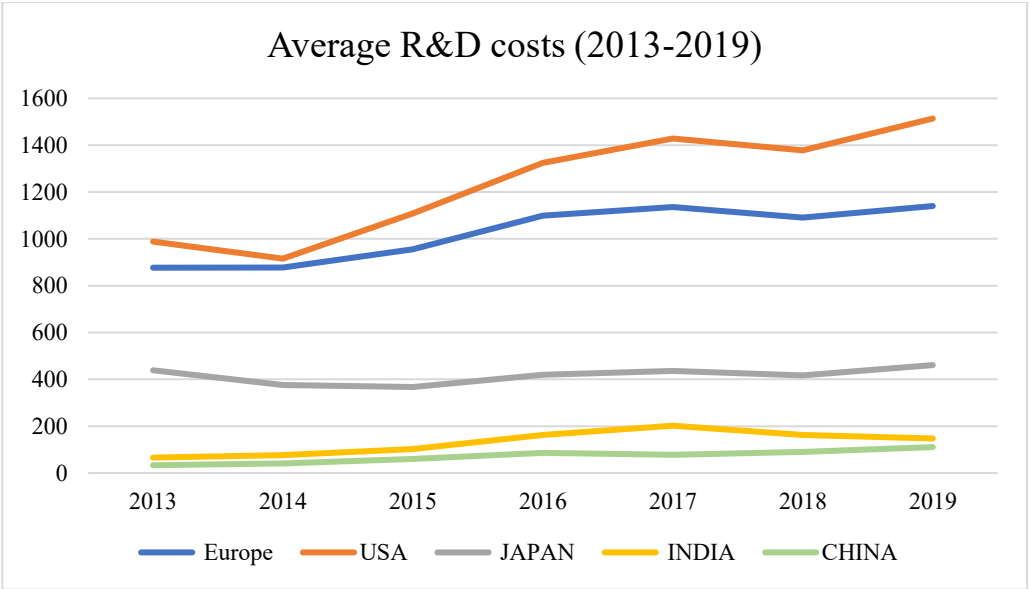

Figure 10: Average R&D costs during the period 2013-2019, in millions of Euros (source: own elaboration)

While the general result from the previous figure apply also in this case, here it appears that the USA spends in average more than any other countries.

Looking at the previous figure from another point of view, i.e. the growth in the R&D expenditures, we can deduce distinct patterns.

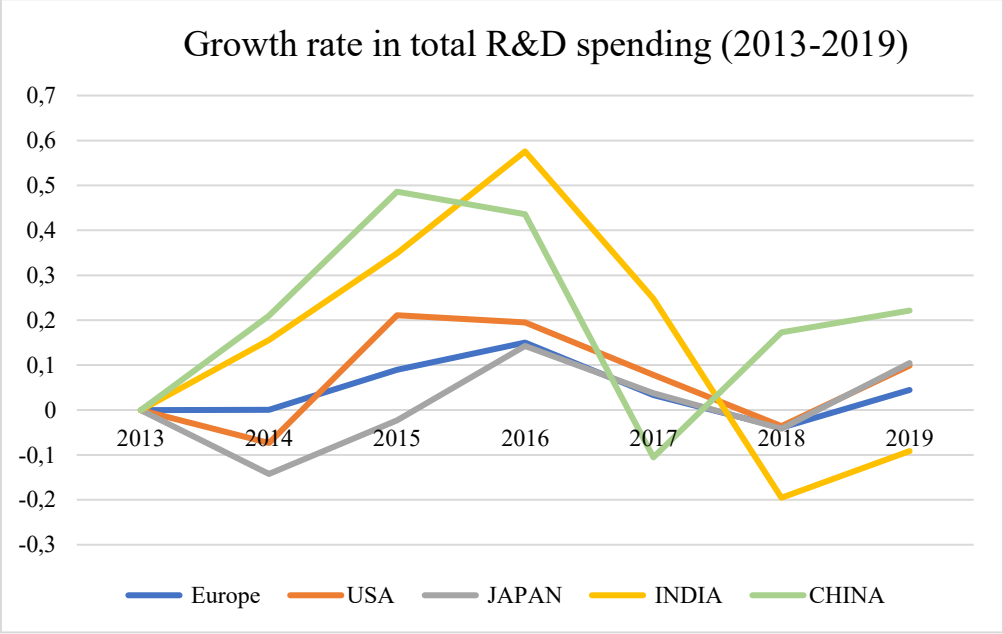

Figure 11: Growth rate in total R&D spending during the period 2013-2019 (source: own elaboration)

From the graph it is clear that in terms of growth in research expenditure, the result depicted in the previous figures is quite the opposite in this case. This is not a surprising result as it is rather obvious that India is a developing country, so as the economy develops so does the pharmaceutical industry. The following figure immediately shows this result.

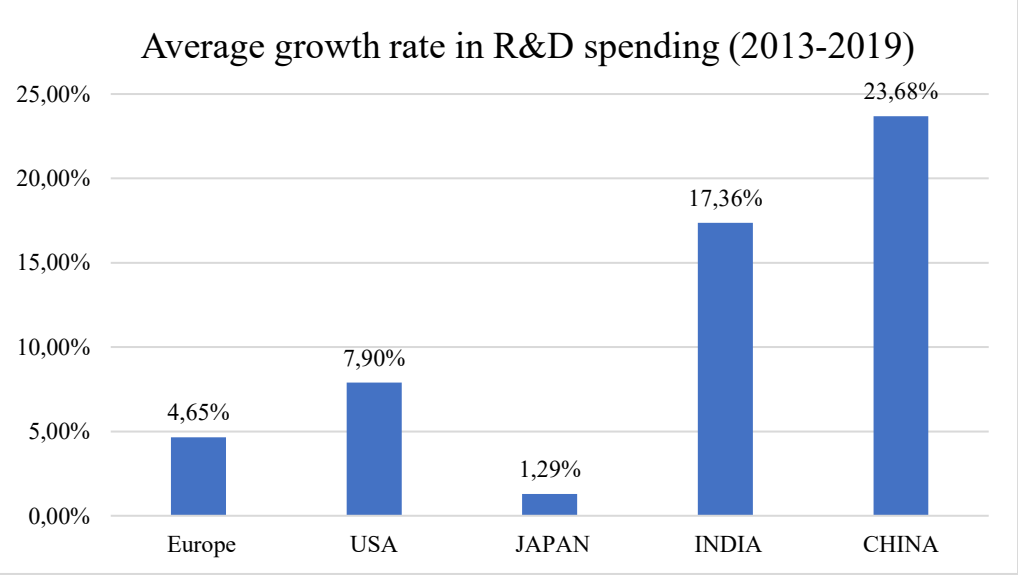

Figure 12: Average growth rate in R&D spending during the period 2013-2019 (source: own elaboration)

Countries like Japan and Europe, but also the USA, have a lower growth in R&D compared to China and India. This is due to the fact that the pharmaceutical industries in the former countries have started their development at the beginning of the 19th Century, hence they are already mature industries. China, and especially India, are countries that have seen their pharmaceutical industries booming during the last decade, therefore the differences in the growth rates are as expected.

It is also interesting to assess the R&D profitability of the countries, focusing particularly on the Indian and European peculiarities. This parameter is calculated as the ratio between the total profit of the country to the total expenditure in R&D, and allows us to determine, in broad terms, how many units of profit are generated by investing in research. We are aware that is a rather indicative measure of how much the profitability of a company is affected by the investments in research, especially considering that each pharmaceutical company has their own specific needs and follows different paths. Nonetheless, it is a measure that is readily available from our database, and it is easy to use for comparison purposes. We can indicate the R&D profitability with the following formula:

$$RDP = \frac{TP}{RDTE}$$

Where *RDTE* is the total expenditure in research and development in each year and TP is the value of total profit for firms in each year.

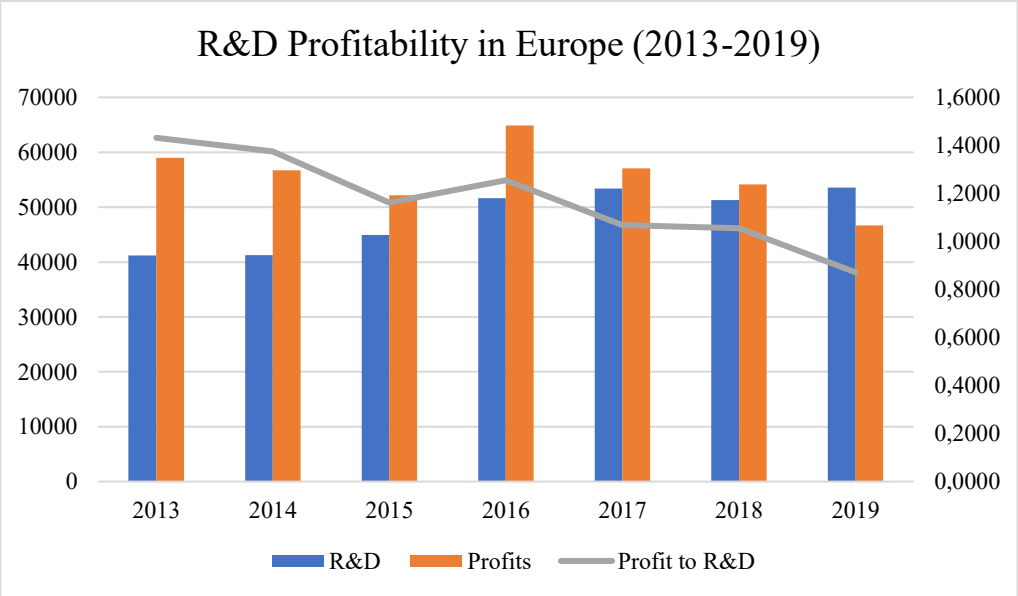

Figure 13: Profit to R&D in Europe during 2013-2019 (source: own elaboration)

It is immediately noticeable that the spending in R&D in Europe has been following a growing path, from the 40 billion of Euros in 2013, but in 2019 this growth has stopped. On the other side, total profits have been more subject to variations during the period, while remaining above the research costs, except for 2019. Furthermore, the average R&D profitability during 2013-2019 has been 1.17, meaning that in Europe, a unit of investment in research, generate, approximately, 1.17 of profit.

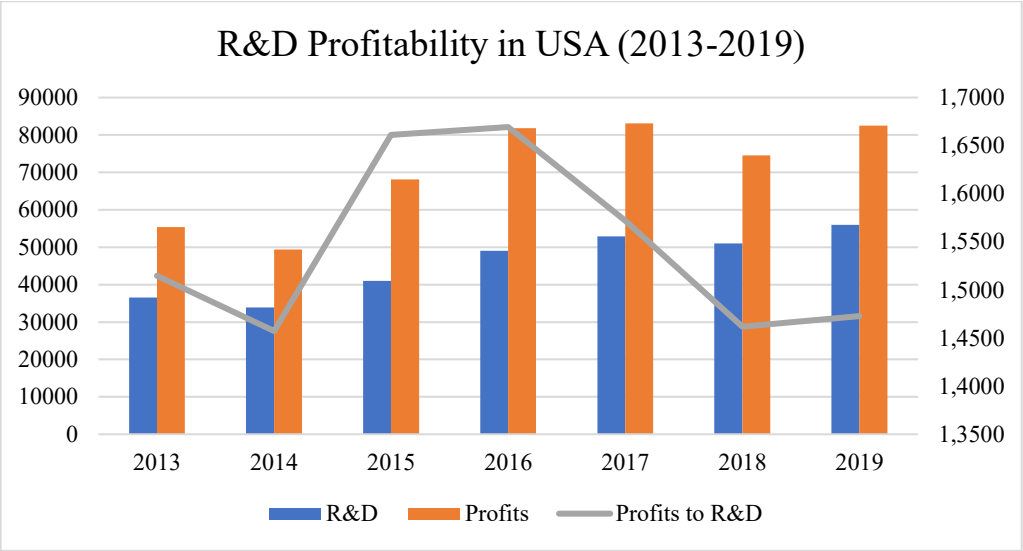

Figure 14: Profit to R&D in USA during 2013-2019 (source: own elaboration)

For what concerns the United States' companies, the R&D profitability follows a different pattern if compared to the previous figure. The main difference here, is that American companies' profits are always way higher than the investment in research, in every year of our dataset. In average, the R&D profitability is higher than Europe, with a value of 1.54.

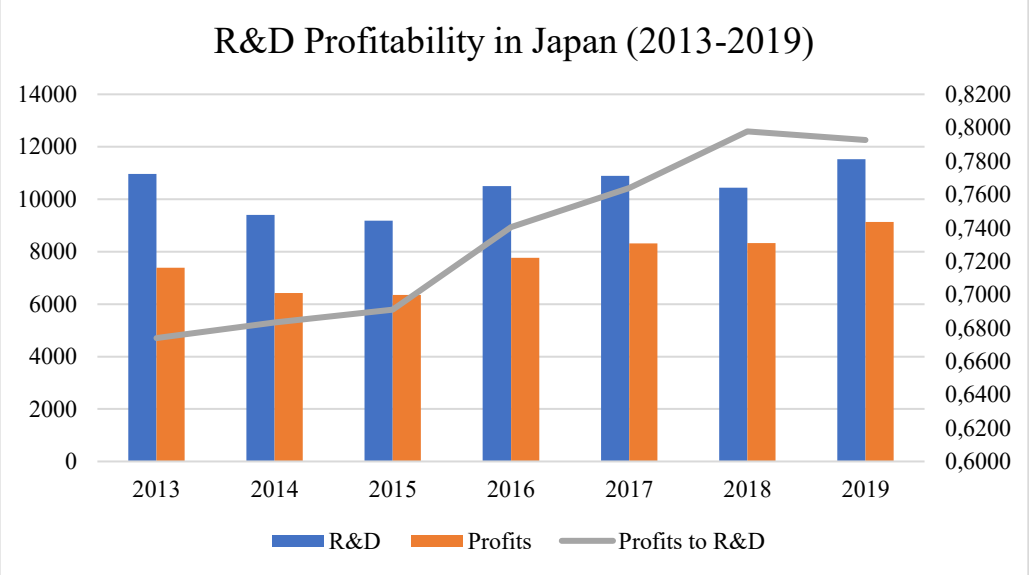

Figure 15: Profits to R&D in Japan during 2013-2019 (source: own elaboration)

The Japanese figure is really interesting considering that the profit is much lower than both Europe and USA, while it would be easy to imagine similar patterns in all three territories, because of the similar economies. Here the average R&D profitability is only 0.73, meaning that a unit of investment in R&D, generate only 0.73 units of profit. This inefficiency is of course affected by the sample size of our dataset, but another sign of this fact could rely on the aspect that Japan is not one of the leading countries in the pharmaceutical industry, as they largely depend on exports.

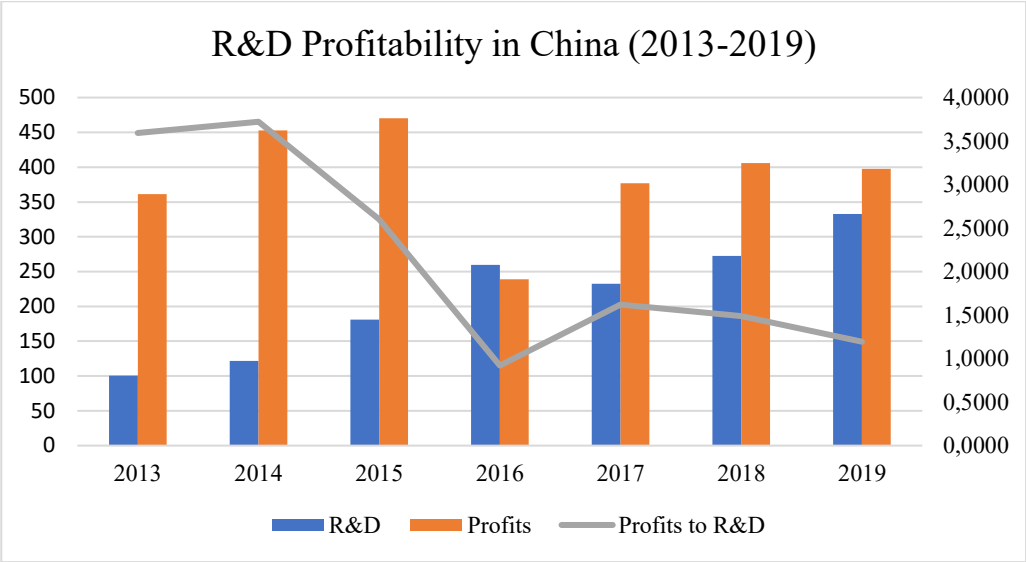

Figure 16: Profits to R&D in China during 2013-2019 (source: own elaboration)

Compared to the previous countries, Chinese companies are profiting more from research, as the average R&D profitability is much higher than Japan, USA and Europe, being 2.16. The figure also shows an impressive growing in R&D expenditure during the last years.

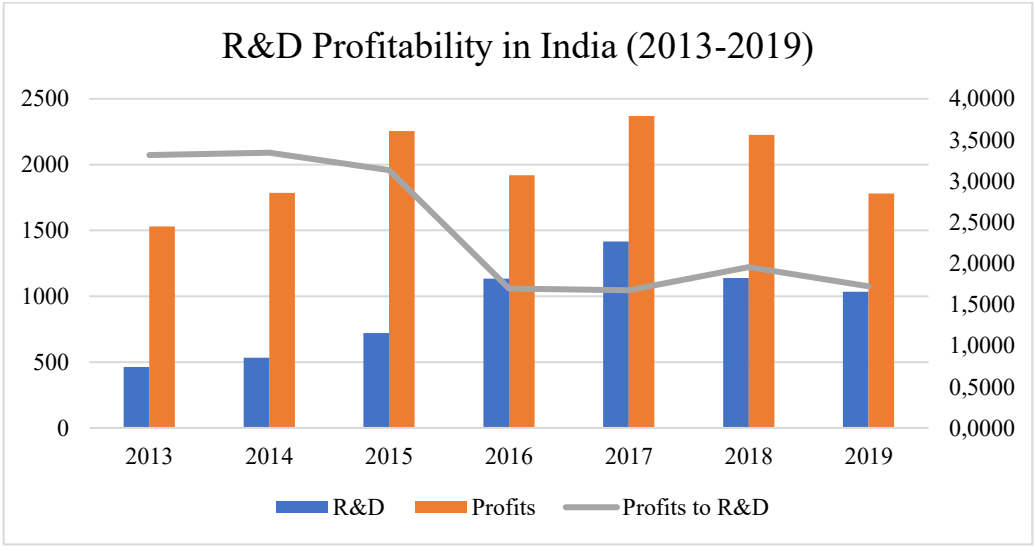

Figure 17: Profits to R&D in India during 2013-2019 (source: own elaboration)

Finally, India's figure depicts a result that is similar to the Chinese case, but with a R&D profitability higher than all the previous country, being 2.40. So, a unit of investment in research, for the Indian companies, can generate in average 2.40 units of profit.

The previous results, while being affected by the sample characteristics and the number of companies in the dataset, immediately allow us to classify the countries from the most productive to the least ones. If compared to the results from the total expenditure in R&D, here we have opposite results. China and India are the countries that have the highest productivity rate in the world, while Japan here is the least productive country.

Another interesting result that is possible to extrapolate from our dataset is the R&D expenditure normalized by the number of employees of all companies in each country, and we can call this new parameter "R&D Efficiency". This is an interesting indicator that can be used to capture the efficiency of research in the countries in analysis, based on the number of employees. We indicate R&D Efficiency as:

$$RDE = \frac{RDTE}{TNE}$$

Where RDTE is again the total expenditure in research and development in each year, and TNE is the total number of employees in each country in each year.

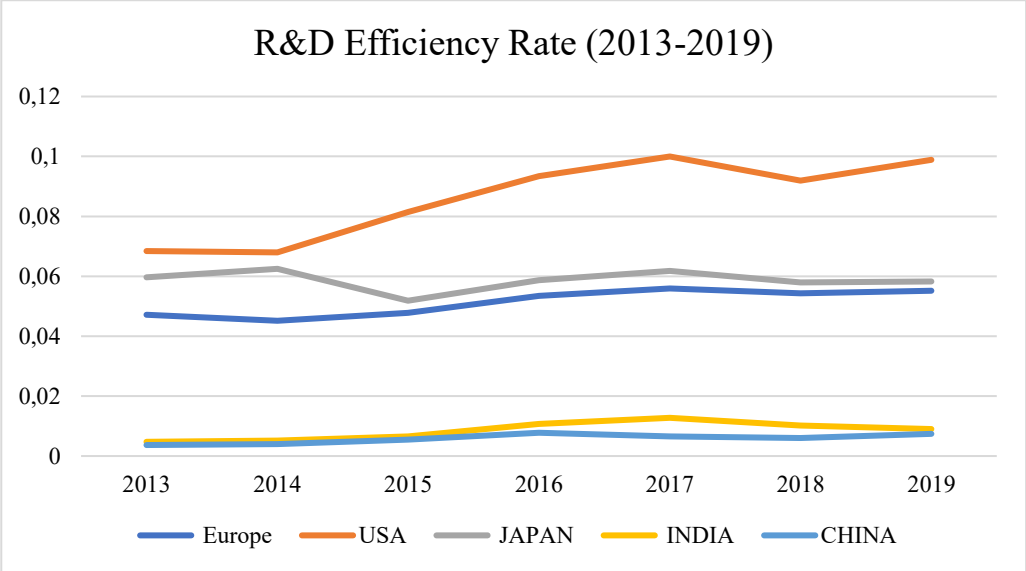

Figure 18: R&D Efficiency rate during 2013-2019 (source: own elaboration)

The most efficient country in the World are the USA, and it seems that their efficiency has been increasing at a considerable rate during the last three years, while the other countries has been maintaining a sort of status quo in this regard. Japan has been consistently more efficient than Europe, which is the third in this figure. India and China are the least efficient countries. This result may be affected by the high population in those countries as well as to the dimension of the companies in the dataset. We understand that this measure cannot really capture how efficient all employees are when companies invest in research, but can give a general idea on the efforts put by the employees in the research and development activities. The next figure depicts the averages for the R&D Efficiency rate.

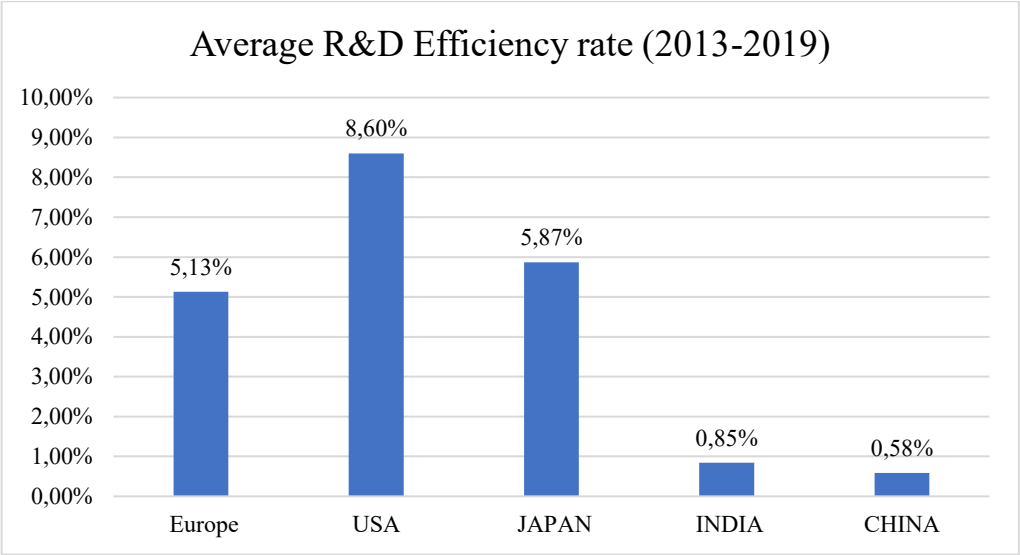

Figure 19: Average R&D Efficiency rate during 2013-2019 (source: own elaboration)

Comparing these results to the R&D profitability, an interesting case study is the Japanese case. With regard to the profitability of research in Japan, it is the lowest among the countries in our dataset, but the efficiency of research is quite similar to Europe and USA, meaning that even if Japan does not profit much from the pharmaceutical industry, their efficiency in research, compared to the number of employees is quite outstanding.

To sum up our analysis of the research and development data in the sample, for the countries considered, we can state few considerations. First of all, Europe and USA have always been the top countries in terms of investments in R&D and total profit. As a result, their profitability has always been higher than one. Second, their spending in research has not been increasing much, as opposed to India and China, which, even though in general terms obtains lower profits and also have lower investments in R&D, have much bigger profitability rates. Finally, the research efficiency rates confirms the American and European leadership in this field, with Japan being the third most efficient country, even though it does not profit much from the pharmaceutical sector.

3.3 Patents in the world

As our dataset contains data of European-based firms, regardless of their country of origin, to maintain consistency, we gathered patents data from the European Patent Office (EPO)[12]. All enterprises are required to request patent grants to the EPO, if they want to patent their product in any European country (unless they want to patent the product only in one European country). We considered the number of patent applications, rather than the number of patent grants, as the latter are more prone to subjective evaluations, and we considered them inappropriate for

[12] Data source: https://www.epo.org/about-us/annual-reports-statistics/statistics.html

our analysis. On the other hand, the number of patent applications are more objective, as they represent the actual effort put by pharmaceutical companies to try to protect and profit from their research and development results.

In the following table, we gathered together data on total patents applications by the same countries contained on our previous dataset: Europe, USA, India, Japan, China, with the addition of the World data.

Table 6: Total patent applications in Europe during 2013-2019 (source: own elaboration)

	Europe	**USA**	**JAPAN**	**CHINA**	**INDIA**	**WORLD**
2013	73,575	34,011	22,405	4,075	562	148,027
2014	75,875	36,668	22,118	4,680	541	152,703
2015	76,194	42,597	21,421	5,728	577	160,004
2016	76,038	40,032	20,943	7,092	761	159,087
2017	78,493	42,463	21,774	8,641	678	166,594
2018	81,594	43,789	22,591	9,480	699	174,481
2019	82,493	46,201	22,066	12,247	637	181,406
TOTAL	**543,972**	**285,761**	**153,318**	**51,943**	**4,455**	**1,142,302**

With no particular surprise, Europe is the first "country" in terms of patent applications, followed by USA and Japan. China is quite behind in this ranking, while India is really on the bottom, confirming its low relevance in the research sector, in particular in the pharmaceutical industry, as we see from the next table.

Table 7: Total pharmaceutical patent applications in Europe during 2013-2019 (source: own elaboration)

	Europe	**USA**	**JAPAN**	**CHINA**	**INDIA**	**WORLD**
2013	2,628	1,815	382	114	9	5,568
2014	2,492	1,815	309	119	7	5,369
2015	2,586	2,257	374	128	8	6,055
2016	2,661	1,962	384	158	7	5,849
2017	2,774	2,316	454	212	9	6,534
2018	3,067	2,651	482	289	10	7,371
2019	3,145	3,026	393	238	11	7,697
TOTAL	**19,353**	**15,842**	**2,778**	**1,258**	**61**	**44,443**

Comparing the total patent applications with the total pharmaceutical patent applications presented to the European Patent Office, we find that the latter account only for 3.89% of the total applications. This means that during the period from 2013 to 2019, a tiny portion of the

patent applications were relative to the pharmaceutical industry. We can find the same information also for the other countries, as depicted from the below table.

Table 8: Total applications and pharmaceutical patents comparison for the period 2013-2019 (source: own elaboration)

	Europe	**USA**	**JAPAN**	**CHINA**	**INDIA**	**WORLD**
Patents applications (Total)	543,972	285,761	153,318	51,943	4,455	1,142,302
Pharmaceutical patents applications	19,353	15,842	2,778	1,258	61	44,443
Pharmaceutical/Total	**3,56%**	**5,54%**	**1,81%**	**2,42%**	**1,37%**	**3,89%**

Looking at the percentages above, USA is the country that applies for more pharmaceutical patents compared to the total patent requests. India and Japan are the countries that request fewer pharmaceutical patents, but for two different reasons. India is a country that in general does not depend a lot from patents, especially in the pharmaceutical industry, as mentioned in Chapter Two, because of the high specialization of the generic industry. Japan, on the other hand, applies for a considerable number of patents but in different industries, since does not have a highly developed pharmaceutical industry, if compared to Europe, USA and India.

Using the previous data, but considering them annually from 2013 to 2019, it is possible to bring a new parameter at the table, that we can call "Pharma Intensity" and we define it as:

$$PI = \frac{PPA}{TPA}$$

Where *PPA* is the number of pharmaceutical patents applications and *TPA*, is the total pharmaceutical applications.

Table 9: Pharma Intensity during 2013-2019 (source: own elaboration)

Pharma intensity	**Europe**	**USA**	**JAPAN**	**CHINA**	**INDIA**
2013	0,0357	0,0534	0,0170	0,0280	0,0160
2014	0,0330	0,0495	0,0140	0,0254	0,0129
2015	0,0339	0,0530	0,0175	0,0223	0,0139
2016	0,0350	0,0490	0,0183	0,0223	0,0092
2017	0,0353	0,0545	0,0209	0,0245	0,0133
2018	0,0376	0,0605	0,0213	0,0305	0,0143
2019	0,0381	0,0655	0,0178	0,0194	0,0173

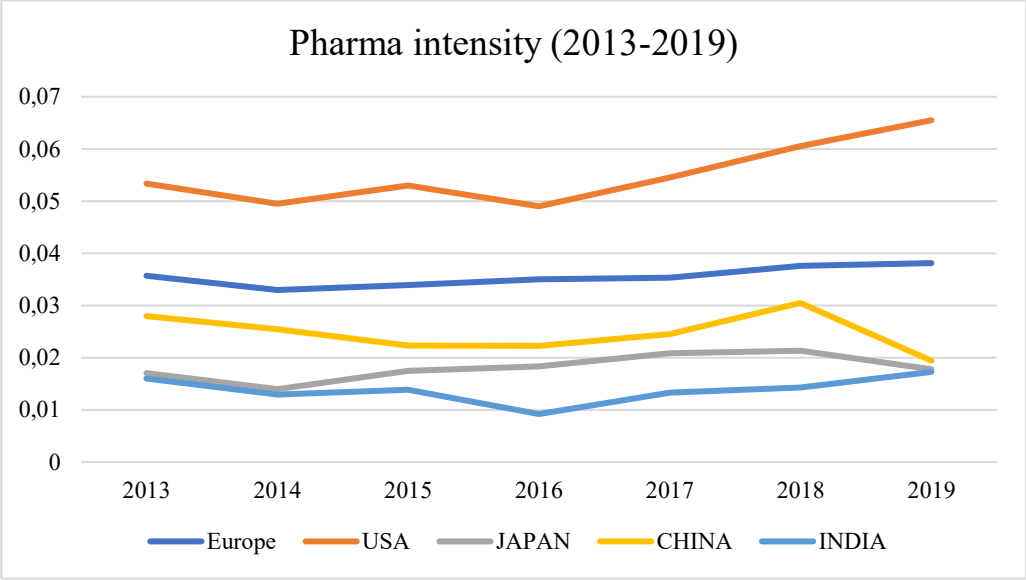

Figure 20: Evolution of the Pharma intensity during 2013-2019 (source: own elaboration)

The table and the figure above confirm the results stated beforehand, but it is surprising to note that the USA and India have seen their index growing after 2016, while the other countries have been more or less constant, since 2014.

For our purpose, it is compelling to introduce another parameter, that derives from the previous pharma intensity. We would like to weigh our index, to the World's pharma intensity, to find out how much a specific country concentrates their economies on the pharmaceutical industry, with respect to the entirety of our data. We have two different ways to approach the "weighting process": one involves using the total patent data, including the country we want to weight, and in the second approach we remove the country from the total patent data. We will show both approaches, and see that they do not differ so much, especially in the Indian Case.

First of all, we define the new Specialization Index as:

$$SPEC = \frac{\frac{PPA}{TPA}}{\frac{WPPA}{TWPA}} = \frac{PI}{WPI}$$

Where the numerator is the Pharma Intensity defined before, and the denominator is composed respectively by the world pharmaceutical patents applications (*WPPA*) and the total world patents applications (*TWPA*). We define the denominator as World Pharma Intensity index (*WPI*). Furthermore, with regards to the two approaches before mentioned, we call *WPI1* the parameter that includes the country that we want to weigh, while *WPI2* is the parameter that does not include the country in analysis.

In the next table and figure, we find all the specialization indexes for the period 2013-2019, including all the countries in the denominator.

Table 10: Specialization Index (WPI1) during 2013-2019 (source: own elaboration)

Specialization Index	Europe	USA	JAPAN	CHINA	INDIA
2013	0,9496	1,4187	0,4533	0,7437	0,4257
2014	0,9377	1,4078	0,3973	0,7232	0,3680
2015	0,8969	1,4001	0,4614	0,5905	0,3664
2016	0,9518	1,3330	0,4987	0,6060	0,2502
2017	0,9011	1,3906	0,5316	0,6255	0,3384
2018	0,8898	1,4331	0,5050	0,7216	0,3386
2019	0,8985	1,5436	0,4198	0,4580	0,4070

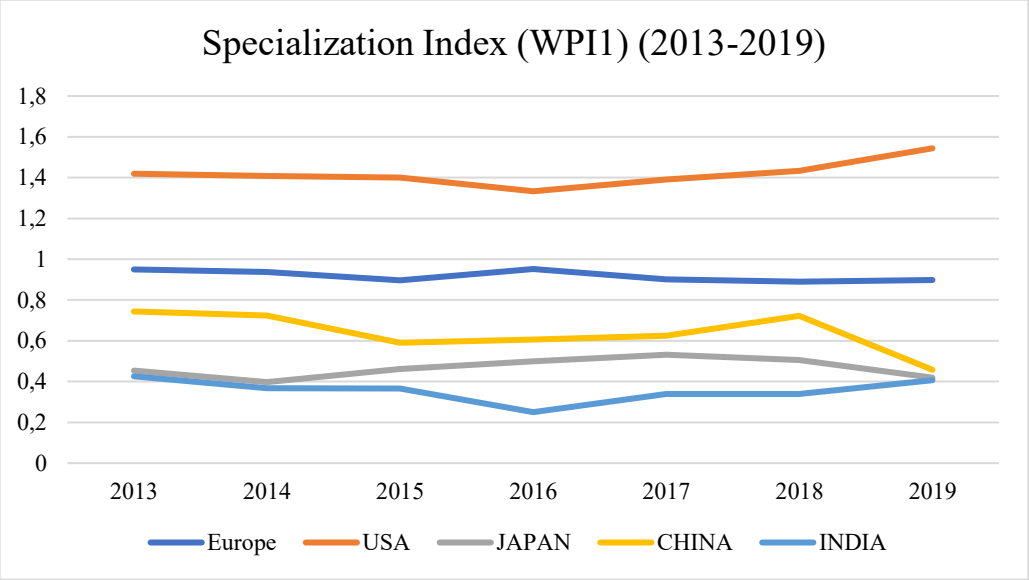

Figure 21: Evolution of the Specialization Index (WPI1) during 2013-2019 (source: own elaboration)

The general result from the Pharma intensity parameter, it obviously applies also here, especially if one considers Figure 20 and Figure 21, since we only divided each Index by the same value on the denominator for every year. What it is interesting here is that we can use this parameter as an important indicator on each country's specialization in the pharmaceutical sector. We can state that the following conditions:

- If SPEC>1, the country is more than specialized in the pharmaceutical sector;
- If SPEC<1, the country is less than specialized in the pharmaceutical sector.

If we consider the following figure, showing the average Specialization indexes, we have a clearer picture on the countries' specialization.

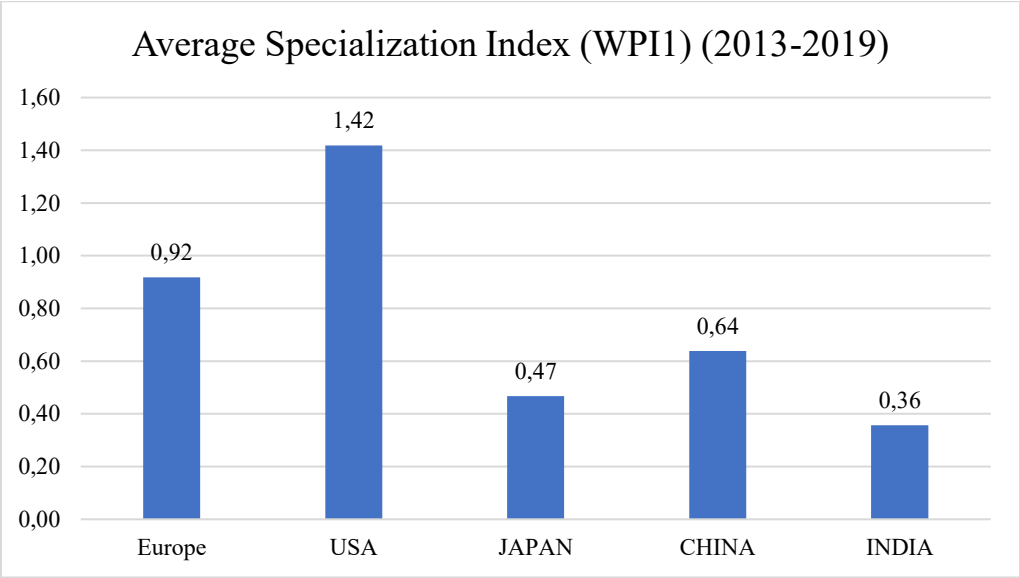

Figure 22: Average Specialization Index (WPI1) during 2013-2019 (source: own elaboration)

The USA is the only country that is more than specialized in the pharmaceutical industry, while Europe's parameter is slightly lower than 1. India is the least specialized country, with a SPEC of only 0.36. Japan and China also are not so specialized in the sector which is an additional confirmation of the result we have found in the previous sections.

Now, we apply the second parameter regarding the world pharma intensity, i.e. WPI2, where we remove from the denominator of the pharma intensity, the country we want to assess. In this way, we can make a better comparison, with no data conflict, since the variable we want to find is not affected by itself.

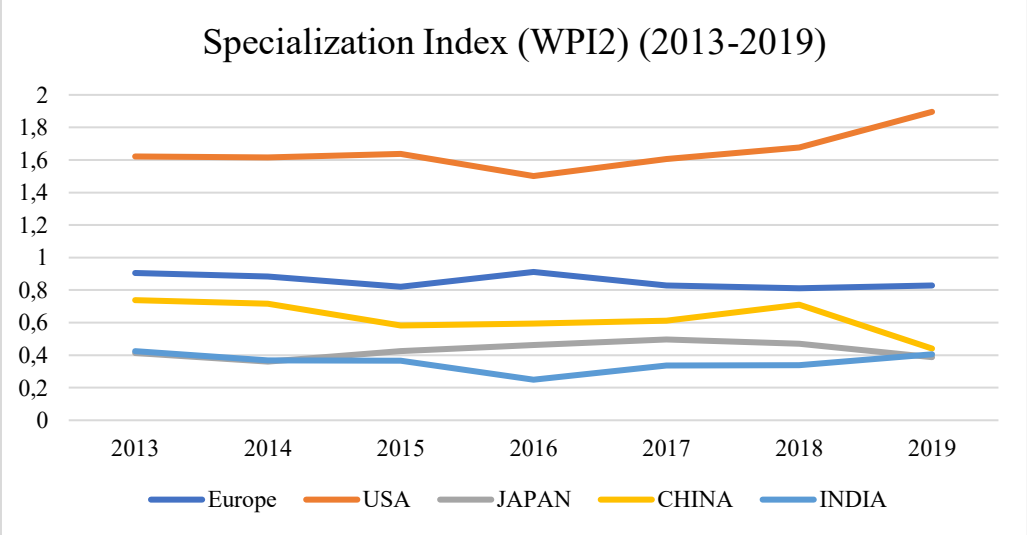

Figure 23: Evolution of the Specialization Index (WPI2) during 2013-2019 (source: own elaboration)

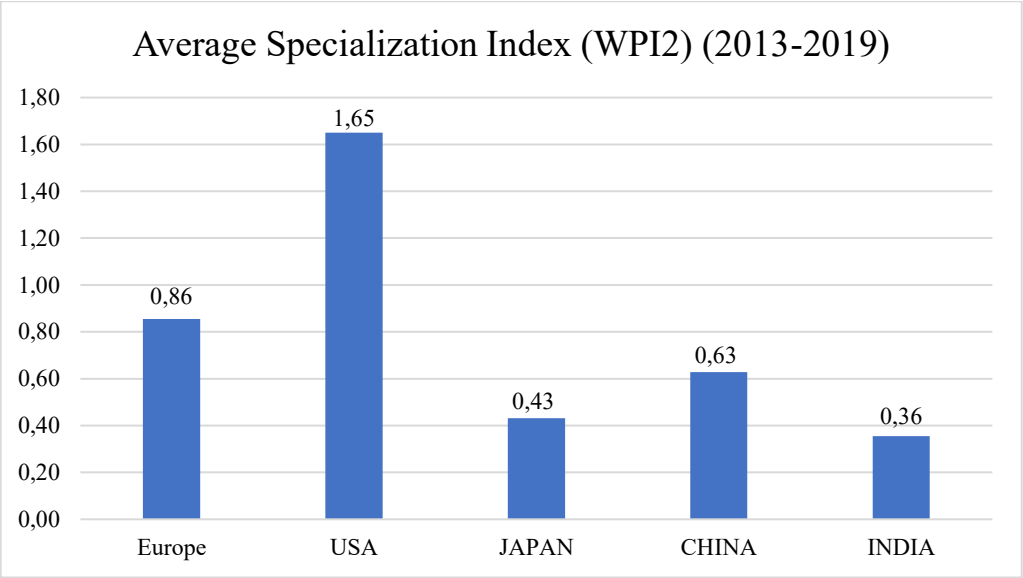

Figure 24: Average Specialization Index (WPI2) during 2013-2019 (source: own elaboration)

In Figure 23, we see no particular differences with the previous results. The only comment worth making is that there has been a general down shift of the indexes. Nevertheless, as the formula of the Specialization Index is: $SPEC = \frac{PI}{WPI}$, if we remove a country from the World Pharma Intensity, it could be immediate to think that the SPEC would lower. However, as the WPI is a ratio itself, the removal of the country affects only the denominator of this ratio, increasing as a result the WPI. In definitive, the Specialization Index, decreases when we remove a country. This result is confirmed by Figure 24, where we see a widespread reduction in the average indexes. The more patents a specific country applied for, the more is the resulting difference of the two indexes, i.e. WPI1 and WPI2. For example, since the number of patents both in the pharmaceutical sector and in the total applications for India are quite small, we see that both parameters are 0.36. On the other hand, for Europe and USA, which had a more sizeable number of patent applications, we find that WPI1 and WPI2 are a little bit different. In any case, we will consider WPI1 for our analysis, as the difference between the two parameters, are quite negligible.

3.4 Indian model applicability

From our analysis of the dataset from the EU R&D Surveys and the data on patents from the European Patent Office, we can make few general comments, in particular on the differences of the country-specific models.

First of all, we find that advanced countries (USA and Europe) are the biggest spenders in research and development in the pharmaceutical sector, while India and China are the countries that invest less, in proportion, in R&D. If instead we consider the average growth rate in research investments from the previous result, we have the opposite scenario. During the period

in analysis, i.e. 2013-2019, China and India have been growing on average, by 23.68% and 17,36% respectively. On the other hand, USA and Europe have been growing at a much lower rate (see Figure 12). This means that, even though their total investments in R&D in the pharmaceutical sector have been much lower than the other countries in the dataset, their average growth has been much bigger during the last years. Therefore, we can expect that the differences in the total investments in research will reduce in the imminent future., when developing countries will reach the first world countries level, at least in economics terms.

Second, we have introduced a parameter which is the R&D profitability (i.e. *RDP*), defined as the ratio between the total profits of the countries and the total expenditure in research and development for the enterprises in each country. In this case, we have a different scenario and we find that the countries that profit more based on their research investments are India and China, with a value of 2.40 and 2.16 respectively. In this case, quite surprisingly, Japan is the country that profit less from their research investments in the pharmaceutical sector, with a value of 0.73. The USA and Europe, have a much smaller value of profitability compared to China and India, being almost the half (1.17 for Europe and 1.54 for USA). Indeed, it is worth noting that India and China, have, as stated before-hand been growing a lot in terms of expenditure in R&D during 2013-2019, This means that, despite the usual theory on India as a country that is mostly specialized in the generic drugs industry - so does not invest a lot of resources in R&D - here we find that the Indian companies do actually invest and are also very profitable, similarly to China.

Third, if we consider the efficiency of R&D in the dataset, defining a new parameter, i.e. *RDE*, as the ratio between each countries' expenditure in research and the total number of employees, we find results similar to the previous points. More specifically, we find that the USA is the most efficient country, with Japan and Europe as the next in this ranking. China and India, probably because of their large populations and firms' size, are not quite efficient.

Moving on with the data on patents from the EPO database, we find that the previous rankings on the research expenditures are more or less confirmed with the number of patent applications. Europe and USA are the countries that request patens to the EPO offices the most, while India does not rely so much on patents. China and Japan request a relevant number of patents, but we will see that their total pharmaceutical patents are not really relevant compared to their total applications.

Indeed, if we compare pharmaceutical patents applications to each country's totals, we have similar results, and in general we have that the former accounts for less than 4%, on average with respect to the total applications. Hence, the relevance of pharmaceutical patents in Europe is not very high during the period we analyzed.

With the previous results, we have established another noteworthy parameter, which we called the "Pharma Intensity", i.e. *PI*. This parameter allows us to measure the impact of pharmaceutical patents applications to the total applications, to assess the "effort" put by each country in the pharmaceutical sector. A higher rate means that the country puts more effort than a one with a lower rate. USA and Europe are the countries that concentrate their efforts in the pharmaceutical sector most, and this is not very impressive as the most important firms in the world, operating in this industry are either from the US or based in Europe.

Starting from the previous result, an additional "improvement" of the pharma intensity index consists in "weighing" the index to the world specialization index. We called this parameter "Specialization Index" (*SPEC*), and it is a double ratio: the first Pharma Intensity, over the World Pharma Intensity (*WPI*). We have defined the latter in two different ways, one in which the country in analysis is included in the WPI parameter (*WPI1*), and one in which we have removed it because of consistence purposes (*WPI2*). We find that the differences of the two variables are not very relevant and they do not alter our arguments. Mathematically, the specialization index is a parameter that can take a value higher or lower than one. We have stated that if the parameter is bigger than one, than the country is more than specialized in the pharmaceutical sector, while if it is lower than one, then we have the opposite case.

Our results (if we consider *WPI1* as parameters) tell that the United States is the country with the highest specialization index, with a value of 1.42. The second most specialized "nation" is obviously Europe, but with a parameter much lower than one, 0.92. The country that has the least degree of specialization in the pharmaceutical industry is India.

Now that we have depicted all the results, we have been able to retrieve from the dataset and the patents data from the EPO, we are ready to do a simple regression analysis to reply to our main question: is the Indian model applicable to more advanced economies? More in details, we want to find if a model based on low specialization in the pharmaceutical sector, hence a low world specialization index, is able to stimulate research and being able to generate enough profits to continue their activities, nonetheless. For this purpose, we will see what happens when we let our variables on the R&D Survey dataset, shown in the following table, interact with the weighted specialization indexes and the number of employees (proxy for the firms' size).

Table 11: EU R&D Survey dataset variables

Variables	**Description**
Region	Region of origin of the pharmaceutical firms
Year	The dataset contains data from 2013 to 2019
R&D	Total expenditure in research
Profits	Total profits

Employees	Number of employees for the companies
R&D profitability	Total Profits over total R&D
Specialization index	Pharma intensity over World pharma intensity

In other terms, we want to assess how much the specialization index "affect" the growth in research for the countries. We already have seen that research and development growth in India is not as low as one could think, so it is interesting to understand if its lower specialization in the sector is irrelevant when it comes to the growth of R&D and the profitability. If we are able to verify that patenting strategies are not so relevant when it comes to stimulating research expenditure, then we can presume, very theoretically, that we can apply a patent system such as the Indian one also in more advanced economies, without prejudicing a country's research activities.

3.5 Empirical model

Our simple empirical model has the objective to identify some connections between the research and development profitability and the specialization indexes, using the number of employees as a proxy for the firms' size. In this case, we slightly modified our dataset, with respect to the previous analysis, considering all negative profits as zero. This change affects the following table, where the means and standard deviation of the profit to R&D ratios are shown.

Table 12: Mean and St. Dev of R&D Profitability

Profit to R&D ratio	**Europe**	**USA**	**JAPAN**	**CHINA**	**INDIA**
N° Obs	588	259	175	21	49
Mean	1.265793	1.067493	1.547055	2.16509	2.494302
St. Dev.	1.555801	1.464985	1.26162	1.659855	1.877999

Indeed, from the table above, we see that while Europe, China, and India's means are similar to the ones discussed beforehand, the USA, and especially Japan, have seen their averages change. This is of course due to our modification of the negative profits on the dataset, but for our analysis, these changes in the countries' means does not affect the general results.

Our empirical model considers the relationship between the R&D profitability, that is a measure of the "productivity" or "profitability" of a country in the pharmaceutical sector, and the specialization index of each country, that can be assumed to represent the "business model" of a country. We also added the employees' numbers to take into account the firms' size. It is important to state that the two measures are expressed in very broad terms as productivity and

business model indicator, and we are aware that they are not totally representative of the reality. However, they are the best indicators that we have been able to retrieve from the (few) data that we managed to gather together. We can write our model as the following equation:

$$\ln(RDP)_{it} = \beta_1 lnSPEC_{ct-1} + \beta_2 lnEMP_{it-1} + \alpha_i + \delta_t + \varepsilon_{it} \qquad (1)$$

where (*RDP*) is the profit-to-R&D ratio of firm i in year t, *lnSPECct* is the (natural log of) pharmaceutical specialization index, computed as the ratio between the share of pharmaceutical patents in country c in year t and the corresponding share computed at the world level, *lnEMP* is the (natural log of) firm's total employment, used as a proxy of firm size, while αi, δt, and εit are, respectively, the vector of firm-specific fixed effects, the vector of year-specific fixed effects and the stochastic error component.

Equation 1 is estimated using a fixed-effects estimator with standard errors clustered at the firm level, as we are only interested in analyzing the impact of variables that vary over time. The fixed-effects estimator has been used also because we cannot assume that firms' parameters (for example the employees' number) are random and uncorrelated with the independent variable in the model, therefore it is more suitable than the random-effects estimator. In addition, we do not have reasons to believe that differences across entities have some influences on our dependent variable. In the following estimates' table, we have additional confirmation of the correct use of the fixed-effects model, as the R squared within groups are always higher than the R squared overall.

Table 13: The profit-on-R&D returns of pharmaceutical specialization (fixed effects panel estimates)

DEP VAR: ln(RDP)	(1)	(2)	(3)	(4)
$\ln(SPEC)_{t-1}$	0.668**			
	(0.210)			
$\ln EMP_{t-1}$	0.060	0.059	0.058	
	(0.042)	(0.043)	(0.043)	
$\ln(SPEC\ EU)_{t-1}$		0.035	0.345	
		(0.916)	(0.569)	
$\ln(SPEC\ India)_{t-1}$		1.179**	1.142**	1.162**
		(0.366)	(0.357)	(0.361)
$\ln(SPEC\ USA)_{t-1}$		0.910		0.773
		(1.612)		(0.938)
$\ln(SPEC\ Japan)_{t-1}$		0.148		
		(0.265)		
$\ln(SPEC\ China)_{t-1}$		2.193***		
		(0.155)		
Year dummies	Yes	Yes	Yes	Yes
Constant	0.358	0.277	0.312	0.259
	(0.338)	(0.373)	(0.372)	(0.386)

N	714	714	714	714
R^2 within	0.055	0.074	0.057	0.058
R^2 overall	0.004	0.010	0.000	0.003
Nr. cluster	119	119	119	119
VIF	1.49	29.18	1.44	1.45

Firm-level clustered standard errors in parentheses * $p < 0.10$, ** $p < 0.05$, *** $p < 0.001$

Looking at the table, we have in the first column the estimates from Equation 1, and we immediately notice that our specialization index has a statistically significant positive relationship with the profit to R&D ratio. This means that a positive variation of the specialization index results in a positive variation of our dependent variable, and vice versa.

In the second regression, instead of considering the world specialization index, we considered each country's specialization indexes to identify the differences between the Indian and European firms. All specialization indexes are positive, but only India and China have statistically significant estimates, which are also much higher than the other ones. Unfortunately, as the VIF (Variance Inflation Factor) test is quite high, it means that there is a high degree of multicollinearity, so in columns 3 and 4 we remove some of the independent variables and focus on the Indian case. In column 3 our main independent variables are the Indian and European specialization index and see that the VIF test result is quite low, so there is almost no multicollinearity, and also that the estimates are more or less unchanged compared to column 2. The previous result is also confirmed by column 4, where instead of the European specialization index, we consider the American one. In both columns 3 and 4, Indian estimates of the specialization are statistically significant and much higher than European and American estimates. In general, from our estimates, we find a positive relationship between the profit to R&D ratio - the productivity/profitability indicator - and the specialization index, which instead is the "business model" indicator. As the Indian estimates are quite high, we can presume that even if the country is not very specialized in the pharmaceutical sector, its productivity is quite high, nonetheless. In other terms, even if India is more specialized in the generic drugs industry, and request fewer patents as a consequence, it's still able to be more profitable than much more specialized countries in our dataset, if we consider the total investments in R&D. From column 3, as an example, we see that a 1% increase in the Indian specialization index would generate a 1.14% increase in the productivity, while the European index would generate a 0.06% increase.

CONCLUSION

The pharmaceutical sector is an industry where reconciling private and public interests at the same time is one of the hardest jobs in the world. We have seen that TRIPS, as the principal instrument to regulate and somehow control intellectual properties around the world - where world means all the countries part of the WTO – has been subject to numerous critics, from those who thought that the Agreement would have endangered underdeveloped countries, but also positive feedback, especially from those who consider intellectual property protection as the main instrument to stimulate research and development. Focusing in particular on patents, which are the most relevant intellectual property tool in the pharmaceutical industry, they must possess, according to TRIPS, three key features: novelty, usefulness, and non-obviousness. Even if these three characteristics could seem reasonable from a neutral perspective, it is worth noting that they have no clear definition in the TRIPS Agreement, so it is a matter of interpretation of each national patent office. This reason, together with the fact that each country that wanted to enter or remain in the WTO had to oblige to TRIPS and establish uniform rules for intellectual property protection, led to lots of discussion around this matter. As of 2020, only the countries listed as LDC's[13] by the United Nations are exempted until 2033 from complying with TRIPS, but the Agreement has been compulsory for the other countries. As it entered into force in 2004, after several years of negotiation, it forced all countries to create a uniform patent system. All advanced nations, like the US and the European Union, already had established quite stable patent systems over time, so they did not have to change their patent laws quite much. On the other hand, developing countries were often forced to radically modify their patent systems to comply with TRIPS. One of those countries was India, which has always been one of the nations with the strictest patent system, in the sense that requesting a patent in that country has always been very difficult. The main reason for this strictness was due to the fact that India tried to protect its critical generic drugs industry and to maintain the role of "pharmacy of the third world". Since it was impossible for the country to refuse compliance with the TRIPS Agreement, they established a specific section on the Indian Patents' Act to circumvent the Agreement to increase public health protection.

Furthermore, we compared European and Indian patent systems, and we found that, even though they have similar evaluation criteria (which is obvious if you consider that they all are countries part of the WTO), the procedures to request a patent are quite different. While in Europe we have a uniform system and also quite inexpensive, in India, requesting a patent is

[13] List of LDC's countries available at: https://unctad.org/topic/vulnerable-economies/least-developed-countries/list

very hard and impossible to perform if you are not assisted by professionals. Indeed, according to Indian patent laws, you must fill out almost 20 different applications and provide a huge number of documentations. In Europe, the procedure is simpler as everything is done through an online portal. Last but not least, in India, if you consider the average wealth of the population, it is very costly to request a patent, and also to renew it before it expires. Applying for a patent is much less costly in Europe, and both the application procedure and the costs will reduce further when the Unitary Patent is introduced in 2021.

Because in this thesis our objective was to understand if a model characterized by a low R&D specialization in the pharmaceutical sector (e.g. low patent requests) and a strict patent system, like India, can be applied to a more advanced economy, like Europe, maintaining at the same time a good level of productivity/profitability. For this purpose, we first studied the European and Indian pharmaceutical industries. Unsurprisingly, in Europe, there are countries like Switzerland, Germany, Switzerland, and the UK that invested almost 30 billion Euros in R&D in 2018 (according to EFPIA). India's data was not available, but according to IBEF, the country's investment in research in 2018 has been estimated to be more or less 8% of the total revenues, which was 18.2 billion dollars in that year. So, the difference between the two areas is quite sizeable. Another interesting distinction between Europe and India is that in proportion, Indian companies invest a higher percentage in research compared to their profits. In addition, the higher investments in R&D in European countries is more than compensated by their profits. Furthermore, Indian industry size (in terms of sales) and investment in R&D have been growing a lot in recent years, so Europe, but also the US, should expect that in the next years, the difference between the countries will reduce more and more. Finally, Indian specialization in the generic drugs industry is corroborated by the data, showing that more than 70% of the pharmaceutical industry is devoted to that field. However, it is interesting that few countries in Europe, such as Italy, reach similar percentages for the generics industry, even though on average the entire generic industry in Europe is not quite as large as the Indian one.

As mentioned before, we also compared the European and Indian patent systems numerically, and have seen that there are some important differences. In Europe, during 2010-2019, the number of pharmaceutical patent applications has been consistently over 5000, with at least 1000 approved each year. In India, however, we have much fewer requests for patents, and also minimal quantities of patents have been approved, confirming the stricter patent laws.

After distinguishing Indian and European models, we gathered research and development data from the EU R&D Survey, which contains data from the 2500 companies that invest most in

R&D in Europe[14], for the period 2013-2019. After the selection of European, American, Japanese, Chinese, and Indian firms, we selected a few key variables and performed a descriptive analysis. First, we found that European and American firms invest most in R&D but have much lower growth rates in R&D expenditures than Chinese and Indian firms. In numerical terms, India's average growth rate in R&D investments during 2013-2019 has been 17%, while the European one has been 5%. Second, we defined a new parameter that we called R&D Profitability (*RDP*), which can be interpreted as a productivity parameter, that shows how much a country profits from investing in research and development. We found that the most productive countries are India and China, while Japan is the least productive. This result is outstanding if we think that India is seen as a country that is not considered a great innovator, but here we have that its research investments are very productive. Third, we assessed the efficiency of research in each country, defining another parameter, which we denominated R&D Efficiency (RDE), that relates the number of employees and the expenditure in research and development. Here, we have that the most efficient countries are USA, Europe and Japan, while China and India, are the least efficient ones, probably due to the firms' size.

Since we were also interested in studying the patenting strategies of the countries in the dataset, we extracted patents data from the European Patent Office (EPO) database. We found that during 2013-2019, more than 1 million patent applications have been presented to the EPO. However, only a small portion of them were pharmaceutical patents, less than 4%. The countries that have requested most pharmaceutical patents are the USA and Europe, which is not a surprise. On the other hand, India requested less than 100 pharmaceutical patents during the entire period, confirming its predilection for the generic drugs industry. With these data, we defined an interesting measure, the Pharma Intensity (*PI*), that measures the share of pharmaceutical patents of a country with respect to the total applications. Since this measure is not very interesting by itself, we have "weighted" it with the world value. The new Specialization Index (*SPEC*) allows us to assess each country's specialization in the pharmaceutical sector. The most specialized country is the USA, followed by Europe and China, and India, again, is the least specialized country.

Our empirical model tried to shed light on the inconsistency between the low specialization in the sector and the high profitability of the Indian pharmaceutical companies. The model had the objective of finding a relationship between the profit-to-R&D ratio and the specialization index. Our fixed-effects model showed a positive and statistically significant relationship between the two variables. A positive increase in the world specialization index results in a positive variation

[14] It is important to note that all firms in the dataset are based in Europe, regardless of their country of origin.

of the profit-to-R&D ratio. When we look at the specific countries, we find that India's estimates have always been statistically significant and much higher than both the American and European estimates. Therefore, an increase in the Indian specialization index could increase the country's productivity, more than what would happen in Europe and USA. To conclude, this result contradicts the usual views of India as a country that solely depends on the generic drugs industry and does not invest in R&D because of their low profitability. Instead, our data suggests the opposite. Nevertheless, it is important to say that we have not found a direct causality between the variables, and our assumptions have been quite loose. Anyhow, a system like the Indian one, characterized by low specialization in the pharmaceutical sector but high productivity, may be considered as a good example of operating in the industry without denying poor populations access to fundamental medicines, requesting unethical patents. In addition, India has also been the second country in terms of growth in the pharmaceuticals research and development expenditure, but the patenting requests have not increased at all. This could show to those who justify patent protection as the main instrument to stimulate research in the pharmaceutical industry, that in reality, countries like India, that do not patent much, are investing more and more in R&D, nonetheless.

LIST OF FIGURES

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References

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