



An exploratory analysis of patent fencing in pharmaceuticals: The case of PDE5 inhibitors

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ABSTRACT

Firms pursue a number of strategies to appropriate value, including patenting. In this paper I study patent fencing, a specific filing strategy to use multiple related patents to further enhance value appropriation. The paper addresses the pharmaceutical industry, which shows a high patenting propensity and strong lifecycle management activities leading to additional patent filings per drug. Building on an inductive case study, this paper explores the mechanisms behind patent fencing within a novel class of drugs. Patents with offensive blocking potential are primarily filed in the a later stage of the lifecycle and are tied to certain categories of patents with a low potential to substitute prior filings economically, while filing of patents with defensive blocking potential occurs more often in the early lifecycle stage. Finally, a model is developed on patent fencing in pharmaceuticals that builds on these patents' characteristics.

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1. Introduction

Firms strive to better appropriate value through a range of activities, including legal measures such as trademarks, copyrights, and patents, and strategies building on secrecy, complexity, and lead time advantages (Arundel et al., 1995; Cohen et al., 2000; Levin et al., 1987). In this context, patents have received much attention (see, e.g., Ceccagnoli, 2009; Ernst, 2001; Markman et al., 2004), providing at least some imitation protection that yields short exclusivity periods on the market before competitors introduce their products, as well as creating higher imitation costs (Mansfield et al., 1981). Because even such short temporal advantages may be highly profitable in pharmaceuticals, where a few patents may protect products with billions of dollars in revenues, and patent protection is particularly effective, the patent propensity is relatively high here (Arundel and Kabla, 1998). In fact, without patent protection, many pharmaceutical innovations would not exist (Mansfield, 1986).

The literature on patenting strategies mentions approaches that use multiple patents to create fences, further enhancing value appropriation (Granstrand, 1999; Rahn, 1994; Rivette and Kline, 2000). To date, however, little is known about how such patent fences are erected and how they interfere with drug lifecycle management, which involves different categories of patents to further

protect a drug, including processes, novel formulations, or indications (Bhat, 2005; Howard, 2007; Hutchins, 2003; Whitehead et al., 2008). Apart from these categories, filing strategies that might play a role when creating patent fences include timing of patent filings, exploiting the complementary or substitutive nature of patents (Cohen et al., 2000; Reitzig, 2004), and designing patents in such a way that they protect from imitation or block competitors (Blind et al., 2006). Although these factors have partially been described in isolation, it is still unclear how they may be used in combination to create patent fences. To date, the ways in which pharmaceutical companies orchestrate their patent filing strategies remain to be fully described.

To elicit which filing patterns are engaged by pharmaceutical firms, I chose an inductive case study method, investigating patenting activities of three firms that each introduced new products within a newly established class of drug. More specifically, I studied the field of PDE5 (phosphodiesterase type 5) inhibitors, with 2010 revenues of approximately US \$5 billion; these products are among the most widely counterfeited in the world. The research setting allowed me to study the patenting activities of a market leader and two followers that introduced their products five years after the first firm introduced its drug, thereby gaining significant market share. The dataset involves longitudinal data that facilitate the understanding of potentially significant temporal patterns in the filing process, while also reflecting attempts to keep both original and generic drug makers at distance. It also allowed me to conduct content analysis of patent claims, eliciting the degree to which patent filings related to substances, processes, or novel

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indications; and, jointly with data from a chemical database, assessing the extent to which blocking of competitors took place.

My findings reveal that in the early stage of drug lifecycle management, patents with blocking potential were primarily defensive in nature, while later patents with blocking potential were more offensive, involving some particular patent categories. The results also show that many patents are formulated in a way that prevents imitation and blocks competitors at the same time, while some allow substituting prior patents from an economical perspective to a higher degree than others. Taken together, these findings enhance the prior literature on appropriation strategies. In addition, I develop a model showing how patent fencing took place, including filing motives, timing, categories of patents, and their potential to economically substitutive prior filings.

The next section of the paper explains the different facets of patent filings in detail, followed by a section on drug lifecycle management. Section 4 introduces the dataset, case setting, and methodology. The case analysis is presented in Section 5. The model derived from the case is presented in Section 6, followed by discussions.

2. Complementary, substitutability, imitation protection, and blocking

Prior work on patent management describes a range of patenting strategies aimed at further appropriating value by building clusters of patents (Granstrand, 1999; Rahn, 1994; Rivette and Kline, 2000). These include blanketing or flooding, where a certain technological space is covered by various patents in a rather unsystematic way; fencing—i.e., filing multiple patents that describe different technological solutions for similar functional outcomes (Granstrand, 1999); surrounding, in which a basic patent is surrounded by a competitor's picket fence, and patent networks, such as a certain setup of a portfolio to enhance its overall strength. Among them, patent fencing is a strategy that has also received the most attention in the scholarly literature (Reitzig, 2004; Ziedonis, 2004).

The Carnegie Mellon Survey (CMS) (Cohen et al., 2000) more precisely defines patent fencing as follows: “[...] fence building involves the patenting, though not licensing (nor necessarily even commercializing), of variants and other inventions that might substitute for the core innovation in order to preempt rivals from introducing competing innovations.” (p. 25). This survey uncovered patent fencing tendencies across a range of industries. While the petroleum, steel, machinery, computer, and electronics industries hardly create any patent fences following this definition, the practice is widespread in the textile, paper, and chemical industries, with intermediate levels in the printing, drug, and medical industries. Filing different patents for a drug is widely perceived as fencing within the pharmaceutical industry (see e.g., European Generic Medicines Association). This may, in particular, involve filings shaped by lifecycle management activities.

The prior literature argues that patents employed for fencing are substitutive (Cohen et al., 2000; Granstrand, 1999; Reitzig, 2004). However, complementarity and substitutability are a matter of perspective: One example is patent A, which relates to substance X; patent B, which relates to a novel formulation 1 of a pill with substance X; and patent C, which protects an alternative formulation 2 of a pill with substance X. So, all patents overlap regarding substance X. From a legal perspective, patents B and C each cover one subdomain of patent A, and patents B and C technologically extend patent A, implying technological complementarity in the relationships A–B and A–C. In addition, the relationship B–C implies technological substitutability. However, one need only possess one of the patents A and B or A and C to block the marketing of the

formulations 1 and 2, respectively, each incorporated into a pill with substance X. So, legally, the patents A and B as well as A and C are substitutes, while B and C are complements (as one needs to possess both to prevent marketing these novel formulations).

At least two important boundary conditions are associated with these perspectives. First, the legal breadth of the overlap between the patents determines the economic impact of legal complementarity or substitutability: let us assume that patent D is a substance patent, and patent E is a patent that claims a particular use of the same substance. Then, following the arguments above, these patents are substitutes from a legal perspective. They, however, might not be substitutes from an economic perspective. If the substance alone can address a market potential across multiple uses of, say, \$100 million, the specific use mentioned in patent E may cover only a market of \$20 million. So while technological complementarity and legal substitutability are given, no full economical substitutability can be achieved.

The second boundary condition is ownership of the property rights. When technological complementarity exists and the patents are usually distributed among different owners, then the situation is frequently described as a patent thicket, with mutual blocking potential of the parties (Christie and Dent, 2010; Clarkson and DeKorte, 2006; Cohen et al., 2000; Reitzig, 2004).¹

Imitation protection is the most important motive for filing patents in the pharmaceutical industry, followed by blocking competitors (Blind et al., 2006; Cohen et al., 2000, 2002). Blocking means that firms write patents in a way so that they are close in nature to patents they already own and use for products, to prevent others from patenting them (Cohen et al., 2000). Blind et al. (2006) describe as defensive blocking as it assures freedom to operate. It may also imply that firms patent to prevent others from using a specific technology, a strategy labeled as *offensive blocking* by Blind et al. (2006). Both approaches mean that the inventions within the patents are not incorporated into products by the blocking patentee. This paper follows these definitions. Other reasons for patent protection that frequently play a role in pharmaceuticals are enhancing one's reputation and obtaining licensing revenues. Preventing lawsuits and using patents in negotiations play a minor role in this industry (Cohen et al., 2000).

3. Drug lifecycle management

The drug development and approval process in pharmaceuticals is long and costly, with only a few substances ever approved to enter the market (Girotra et al., 2007; Mathieu, 2005; PhRMA, 2007). At the same time, few blockbuster drugs provide exceptional returns. Pharmaceutical firms also try to identify synergies in R&D by seeking new medical applications for already developed drugs. This helps save time and costs in the lengthy approval process, as some preclinical tests for the substance can be reused from the previous approvals (Chong and Sullivan, 2007). For instance, Sandner and Ziegelbauer (2008) state that of all the drugs marketed in 2004 in the US, 84 percent had new medical indications approved,

¹ Patent thickets are found particularly in complex technologies such as electrical engineering, including semiconductors, telecommunications, but also optics (Cohen et al., 2000; von Graevenitz et al., 2008). Their existence has received much criticism, and there are various reasons for that. First, Heller and Eisenberg (1998) claim that such a situation would deter innovation and lead to the “tragedy of the anticommons,” where resources such as patents are finally underutilized because of higher transaction costs. Second, the existence of thickets triggers firms to apply for even more patents (von Graevenitz et al., 2008; Ziedonis, 2004), expanding the anticommons dilemma and increasing workload at the patent offices. However, the large patent portfolios created in this context finally help improve the applicants' position in cross-licensing negotiations (Blind et al., 2006; Grindley and Teece, 1997) or facilitate membership in patent pools that altogether overcome hold-up problems here (Heller and Eisenberg, 1998; Shapiro, 2001).

while an additional 6% had novel indications under development. Such a reuse of molecules for novel indications extends market exclusivity, at least for the novel indication. These product strategies are also reflected in patent filings, leading to additional patenting activities that, in general, peak around the time market approval of the first-developed drug is in sight (Sternitzke, 2010). Engelberg (1998) shows that, for top-selling products, about half have obtained a market exclusivity from such additional patents which was longer than legislative bodies originally anticipated for brand-name drugs.²

Competition in pharmaceuticals is fierce; generic drug makers aim at capturing a share of the revenues of original drugs as soon as patent protection ends, introducing bioequivalent products and relying on the approval data for safety and efficacy of brand-name pharmaceutical manufacturers.³ In this case, original drug makers encounter substantial drops in sales (Raasch, 2006). Therefore, they are eager to protect their cash cows as far and as long as possible by securing market exclusivity (highly controversial from a policy standpoint, because it keeps costs for the healthcare system high (Kesselheim, 2007)). Howard (2007) and Bhat (2005) describe, apart from marketing and sales strategies that are difficult to replicate by generic manufacturers,⁴ a number of market exclusivities granted by authorities such as the FDA. These include orphan drug status,⁵ new chemical entity data exclusivity that aims to compensate original drug makers for “time lost” during the drug approval process,⁶ and pediatric exclusivity.⁷

Howard (2007), Hutchins (2003), Whitehead et al. (2008) and Bhat (2005) more specifically illustrate the different categories of patents used, not solely for developing product improvements and line extensions, but also more efficient manufacturing processes, including patents on substances,⁸ new formulations or dosing regimens, novel indications, or chemical processes, altogether broadening the legal scope of the property rights held by the applicants (see Table 1). Those patents that are relevant for a drug are listed in the FDA Orange Book.⁹ Patenting novel formulations or indications leads to the protection of markets that generics may not enter, securing market exclusivity there.¹⁰ While product strategies somewhat determine which categories of patents may

Table 1
Patent categories.

Patent category	Characteristics
Gene or protein sequences	Target sequences can be patented, covering an isolated DNA defining the gene, or the DNA sequence of the protein
Substances	Pharmaceutical substances and compounds may be patented, and new versions of these may receive new patents. For example, new crystals or salts may prove more stable than previous ones, or new isomers may be more active than those already patented
Processes	New manufacturing processes representing enhancements in purity, yield, or costs are patentable; these may contribute to economies of scale of the drug maker
Formulations/dosing	Improvements in delivery of an active compound (for example, new forms that provide better drug solubility) are patentable, as are separate dosing regimens and formats (such as solutions, gels, or chewable tablets)
Fixed-dose combinations	Combinations of drugs in single doses may be patentable; these provide benefits for patients by reducing the number of pills that must be taken in a day
Indications and uses	As further research on a drug reveals new indications and uses of an active compound, each of these may be patentable

Source: Compilation is based on work from Bhat (2005), Howard (2007), Hutchins (2003) and Whitehead et al. (2008).

be filed, the effectiveness of these patents varies (independently from the theoretical market potential of the related products), and their linkage to the fencing strategies as illustrated in the previous section is unknown. Without strong patent protection, an original drug maker would very soon face generic competition,¹¹ making it very difficult to recover profits from its inventive activities. Gorlin (2008), for instance, demonstrates a case where specific patents in place laid the groundwork for further successful line extension efforts by a large pharmaceutical company. Hence, strong patent protection is a necessary condition for being successful with line extensions.

Howard (2007) looks at patents in greater detail and argues that it is reasonable to file patents on molecular forms, formulations, processes, and uses about five to ten years after patenting the basic molecule, and to start filing more formulations, dosing patents, and other claims (e.g., preferred crystals) around the approval of the drug, while these patent filings are predominantly used to keep generic competition at a distance.

In the market environment, competitors such as large pharmaceutical incumbents introduce substitutive products which, if possessing superior characteristics some time after market entry of the first-in-class drug, often may gain significant market share (Berndt et al., 2003; Cockburn and Henderson, 1994). It has been reported that during the 1990s, competition intensified within drug classes, a circumstance implying that two or more competitors are working on similar novel drugs in parallel (DiMasi and Paquette, 2004).

So far, the literature stream on complementary and substitutive patents is weakly related to the one on imitation protection and blocking as primary patent motives. However, these reports are even more weakly coupled with the literature on drug life-cycle management and the underlying patenting strategies, such

the medical benefits of the novel formulation. Otherwise, physicians are frequently reluctant to switch patients, prescribing the generic product instead (Gorlin, 2008).

¹¹ Independently from patent protection, the FDA grants three years of market exclusivity for novel uses or novel formulations as long as further clinical studies have been conducted (Gorlin, 2008).

² An explanation for this observation might be that when the study was conducted, the old US patent terms where a patent was in force 17 years from its granting date were still in force, and such patents were finally granted relatively late in the drug approval process, leading to the very long exclusivity periods.

³ They may file an Abbreviated New Drug Approval (ANDA) according to 21 U.S.C. §355 (j) (2) (A) (vii).

⁴ For example, building a strong brand, providing additional product support such as blood tests, or keeping intense relationships with physicians. These measures are difficult to accomplish by generic manufacturers because of the low margins of their business.

⁵ In the US it is possible to obtain seven-year orphan drug market exclusivity for drugs targeting diseases that affect fewer than 200,000 people throughout the country.

⁶ Such exclusivity provides up to five years of additional market exclusivity after patent expiration, expanding market exclusivity in combination with the patents up to 14 years (in the US, Hatch Waxman Act) or 15 years in Europe, using so-called supplementary protection certificates there. In the US, such exclusivity is only available for one single patent from the so-called Orange Book.

⁷ As pediatric studies are frequently neglected, the FDA rewards such work with an additional market exclusivity of six months.

⁸ Not all substance patents filed later are equally effective. Many salts of a substance are not regarded as non-obvious over the first substance patent claimed. It is difficult to infringe on metabolite patents, as metabolites are synthesized in the human body based on the active ingredient of a drug. However, enantiomers (chiral substances), particularly when showing unexpected pharmacological properties, and polymorphs (various crystal forms of a substance) may constitute strong patents (Agranat and Wainshtein, 2010; Gorlin, 2008; Paine, 2002).

⁹ Drug makers list these patents in the Orange Book without examination by the FDA. Process patents may not be listed therein.

¹⁰ However, switching patients to a follow-on product with, for example, a novel formulation works effectively only if head-to-head clinical studies clearly show

as the temporal filing patterns of various patent categories drafted in a way to shield a product portfolio from being imitated by competitors as long as possible. It is, for instance, unknown how far blocking occurs in this context. This paper strives to close the gap by studying the structures of patent filings, eliciting ways that patents were formulated to erect a fence, taking into account various patent categories, imitation and blocking potential of the filings, their complementary and substitutive nature, and temporal patterns.

4. Field of research, data and methodology

As the linkages between the topics to be studied are not well understood, I chose a case study design that will inductively develop a model, jointly with findings from the prior literature, on how these topics interact. Such a case study design is frequently used for qualitative research (Eisenhardt, 1989). Although there are limits to generalizing the results of a case study, this research design allows for a more complete understanding of the intent behind erecting patent fences around important drugs. It does so through the study of the patent claims, which goes beyond quantitative empirical research relying solely on bibliographical data in machine-readable format. The case involves a novel class of drugs where the first patentee could naturally stake its claims; for instance, by creating patent fences. The class further includes one of the most widely counterfeited products in the world, for which the incentives to appropriate value should be particularly high. Choosing such an extreme case makes it possible to carve out key mechanisms (Eisenhardt, 1989; Pettigrew, 1990) that may play an important role for erecting patent fences.

4.1. Field of research

This paper focuses on PDE5 inhibitors, which moderate smooth muscle relaxation by blocking a substance called cyclic guanosine monophosphate (cGMP). Before any compounds in the field were developed, basic research showed that nitric oxide (NO) stimulates the production of cGMP, moderating the effect of smooth muscle relaxation, which results in vasodilation (i.e., widening) of arteries and, consequently, an increase in blood flow. The goal of industrial R&D on influencing blood flow in arteries, which started in the mid-1980s, was to find a drug that could treat patients with angina pectoris or hypertension. It was in the laboratories of Pfizer Ltd. in England where a substance called sildenafil was identified as a PDE5 inhibitor. At the outset, it showed no promising results for the original indication of angina pectoris. But soon, researchers discovered that the drug could treat male erectile dysfunction (ED). The substance, widely known by the brand-name Viagra (sildenafil), was finally introduced to the market in 1998 and is one of the most recognized and most counterfeited products in the world (Business Week). The discovery of this drug is described in Katzenstein and Grossman (2001) or Trott (2008). As is typical when a new substance class is identified, more than one pharmaceutical firm conducted research in this area. In 2003, two further drugs, Levitra (vardenafil) from Bayer and Cialis (tadalafil) from Lilly, were approved by the FDA, and there are more PDE5 inhibitors marketed outside the US (Dorsey et al., 2010). World-wide revenues for the three substances were approximately US \$5 billion in 2010 (no unusual number for a class of drugs containing blockbuster).

Besides treating erectile dysfunction, research has focused on finding and exploring further uses for PDE5 inhibitors, among them treating pulmonary hypertension and lower urinary tract symptoms (Dorsey et al., 2010).

4.2. Dataset

The analyses build on patent data that are publicly available. To elicit a longitudinal dataset of patenting activity for the novel class of drugs, I had to identify corresponding substances. Therefore, the first step was to search the Science Citation Index to identify a relatively recent paper on this class of drugs, namely PDE5 inhibitors (which is Dorsey et al., 2010). The drugs that succeed the first one in a class are known as “me-too” or “follow-on” drugs.¹² Next, I used databases such as the Merck Index to identify the CAS Registry Number (often shortened informally to “CAS Number”), a unique ID used by the Chemical Abstracts Service (CAS), the largest database provider for chemical information available. This number allowed me to track all patents filed that mentioned the substances identified in Dorsey et al. (2010). Third, because patent families are the basis of analysis, the patent numbers identified were transferred to the PATBASE database, which comprises more detailed patent family information. Next, I narrowed the dataset to those substances that are marketed in the US, namely Viagra, Cialis, and Levitra, and limited it to US patent data and families with priority dates between 1999 and 2005. At this stage, I further refined the data (manually studying the patent documents to assess if they, in fact, center on the substances, or if they primarily refer to different substances that, mainly by coincidence, mention also sildenafil, tadalafil, or vardenafil). This step reduced the dataset to a total of 72 patent families from Pfizer, Lilly, and Bayer, with 46, 11, and 15 patent families each. Bibliographical data were eventually added from the Espacenet database. Patent claims were investigated in more detail for each published US patent document and for the first patent document of a patent family (either an application at the European Patent Office (EPO) or via the Patent Cooperation Treaty (PCT)). In addition, data from the FDA Orange Book were extracted to identify those patent numbers that are pivotal for imitation protection.

4.3. Methodology

I conducted several types of data analysis on patent categories (see Table 1) to elicit temporal filing patterns, structures that allow imitation protection and blocking, and complementarity/substitutability from a technical and economic perspective. The investigations build on bibliographical data, content analysis of the patent documents' claims, and identification of chemical substances assigned to the patent families according to the Chemical Abstracts (CAS) database.

To classify patent families according to substance, process, formulation/dosing, fixed-dose combination, and use patents as outlined in Table 1, I conducted content analyses of the claims, defined by the claims in the priority document of the patent family. A patent was considered to be a substance patent if an independent claim contained a substance only, not combined with a use of that substance, which constitutes a substantial limitation of legal scope. In general, such substance patents cover any use of the substance.¹³ Process patents were classified as such either if they directly used the word “process” or if they described a method to conduct several analytical or chemical synthesis steps. Formulation and dosing patents had to describe the use of various ingredients and dosings.

¹² The term “me-too” seems to be somewhat misleading, as about one-third of these drugs receive priority review by the FDA (DiMasi and Paquette, 2004), indicating that they provide substantial benefits for patients. Therefore, these authors suggest the term “follow-on” drugs instead, subsequently used throughout the text.

¹³ An independent claim with a substance and an indication/use would yield a (substance-) dependent patent which, if held by a third party, may block the use of the pure substance patent for this indication. Filed many years later, it could substantially enhance patent coverage of the substance (but only for the specific use).

Table 2
Key findings.

The majority of patents are filed late in the life cycle, relating to novel dosing, fixed-dose combinations, and novel indications
Only seven patent families of 72 protect the three PDE5-inhibitor drugs by being listed in the FDA Orange Book
Patents with defensive blocking potential are filed early in the lifecycle
Patents with offensive blocking potential are filed late in the lifecycle
Substance, process, and formulation/dosing patents have a larger potential to substitute economically for prior patents, while this potential seems to be lower for fixed-dose combinations and use patents

Combination patents had at least to combine a PDE5 inhibitor plus another active ingredient, and use patents had to name at least one indication. Further, the filing time of the patent families is based on the priority date of a patent family, relying on bibliographical data.

I measured the potential for imitation protection by two approaches: first, explicit imitation protection potential was assumed if the invention is marketed (which is indicated by a listing of the patent number in the FDA Orange Book¹⁴). Implicitly, every patent family may serve imitation protection purposes as long as the invention may be marketed in the future, which naturally leaves some room for ambiguity. In contrast to imitation protection, a high potential for offensive blocking was assumed to exist in all cases where firms claimed substances explicitly marketed by competitors, as could be obtained from CAS data as described above. I further assumed a high defensive blocking potential both when a patent claimed features that are substitutive to other owned patents and when these substitutes were not marketed (as indicated by missing Orange Book listings).¹⁵

Complementary and substitutive patents were uncovered based on studying the claims' content, taking the position of substances within the claims as a reference line.¹⁶ More specifically, for example, I assumed patents to be technologically complementary when there is, for example, a substance patent for tadalafil and another patent for the use of tadalafil for treating an indication. I regarded other substances such as sildenafil as being technologically substitutive for tadalafil. Thus, dosing patents for vardenafil were considered to be technologically complementary to the vardenafil basic patent as well, while looking at several dosing patents in isolation means that each may be a technological substitute in comparison to another.

5. PDE5 patent filings and their structure

I next describe the patterns found in the PDE5 patent filings that will be the basis for the model on patent strategies. The key findings are highlighted in Table 2.

5.1. Temporal filing patterns

The distribution of patent categories in the dataset was studied first (results are presented in Table 3). On average, about two categories per family exist. Approximately 80% of all patent

Table 3
Descriptive statistics: categories of patent families (overlaps possible).

Category of patents	# of patents	
Substance	17	[23.6%]
Process	13	[18.1%]
Formulation/dosage	28	[38.9%]
Fixed-dose combination	28	[38.9%]
Indication/use	57	[79.2%]
Average # of categories	1.99	

families comprise an indication of use. Substance patents are relatively rare, as only every fourth patent family belongs to this category.¹⁷ Process patents appear in about every fifth family. Formulation and dosing concepts, but also fixed-dose combinations are described in about every third patent family.

Fig. 1 depicts temporal patenting activity per category and firm, indicating also when FDA approval of the three drugs took place.¹⁸ Substance patent filings occur over the entire observation period, mainly by Pfizer, while Lilly and Bayer are less active here, having tended to file their patents at an earlier point in time. Some substance patents relate to crystals, or to further developments (i.e., novel chemical chains for the molecular backbone) of the molecular structure of the basic drug patent, which is naturally claimed early. Certain substance filings occur in combination with process patents, where intermediate products of the process are protected as substances. While Lilly and Bayer filed process patents continuously over time, Pfizer did so until 2001. The company claimed formulation/dosing patents from 1997 onwards, whereas Bayer and Lilly started two years later, with a handful of families each. Three dosing patents from Lilly relate to tadalafil, and a fourth seems to be filed explicitly to block Pfizer, as it describes dosing of sildenafil (not tadalafil) for a specific use. Fixed-dose combination patents mainly appear during later stages of the drug lifecycle, as do use patents, usually covering indications of the substances, formulations, etc.

5.2. Patents with imitation protection and blocking potential

Seven of the 72 patent families comprise patents listed in the FDA Orange Book, protecting the drugs from imitation. This includes the first two patent families from Pfizer, where the basic patent is a substance patent, with indications formulated within a dependent claim. Since erectile dysfunction (ED) was not yet claimed in the basic patent, the independent claim of the second patent family covers the use of sildenafil for treating ED. Bayer possesses one patent family with two FDA-listed patents, which are both substance patents, claiming ED in dependent claims as well. Four of the early Lilly patent families can be found in the FDA Orange Book. The basic patent is filed as a substance patent, again with uses mentioned in dependent claims. The other three patent families protect dosing and formulation of the drug. As only seven patent families are responsible for direct imitation protection, the other patent filings may indirectly be so.¹⁹ The temporal distribution of the Orange Book patents showed that they were filed throughout the lifecycle of the drug, while especially later ones might protect potential line extensions.

¹⁴ A study of the Federal Trade Commission showed that the Orange Book sometimes comprises patents that do not cover the marketed products (Federal Trade Commission, 2002).

¹⁵ As one cannot derive definite motives from observing actions, I only measure "imitation protection potential" and "blocking potential" of the patents. Actually, motives may change over time. It may be that patents originally filed to block competitors are later used to generate licensing income from them. However, it is important for drafting patenting strategies to formulate patent documents accordingly that they may function to accomplish such motives. This paper studies these formulations.

¹⁶ In the few cases where no substance was mentioned in the claims, the description section of the patent was also studied.

¹⁷ As there was only one patent family relating to gene or protein sequences, this category was subsequently merged with the substance category.

¹⁸ Subsequently, early patent filings refer to those temporally close to the earliest priority date of the patent family (which, actually, may have multiple priority dates referring also to, e.g., continuation applications).

¹⁹ As process patents are not listed in the FDA Orange Book, there may be more patents explicitly filed for imitation protection.

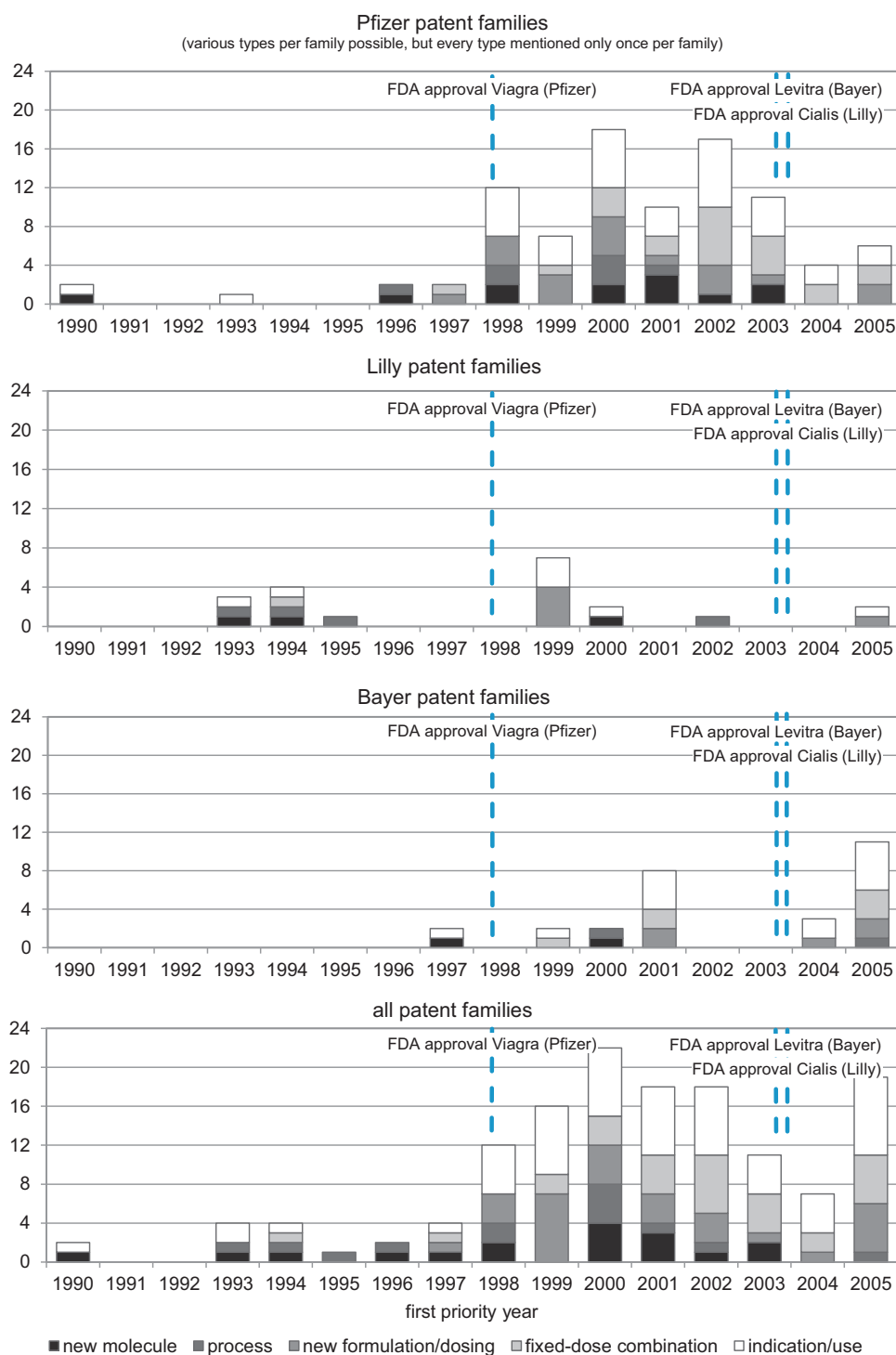


Fig. 1. Pfizer, Lilly and Bayer applying for different patent types over time.

When companies claim applications of substances that are patented and marketed by their competitors, such patents have a strong *offensive* blocking character.²⁰ The results of my analysis

addressing this issue can be found in Table 4. Most of the substance and process patents originate from Pfizer. Some have the potential to offensively block competitors, as they explicitly claim their competitors' substances. However, most of the substance and process patents claim other substances to be used in combination

²⁰ As one reviewer noted, the patents may also have been filed for licensing purposes. In fact, it seems realistic that competitors might show particular interest in obtaining licenses on patents that block their business. At least, during the observation period, none of the patents was actually licensed by a competitor in the sample, as this would have been indicated in the Orange Book. However, the particular intents the applicants had in mind when filing the patents cannot, but also

need not be known, as the structure they chose and that is codified in the patents' claims shows us the potential to block competitors, prevent imitation, etc. Rather, the model to be developed in this paper aims to show how patents were designed in order to fulfill such purposes.

Table 4
Number of patent families per applicant and category (absolute and relative values). Because many patent families comprise documents of various types, overlaps are possible.

Patent category	Company	Absolute values				Share			
		Total	Sildenafil	Tadalafil	Vardenafil	Total	Sildenafil	Tadalafil	Vardenafil
Substance	Pfizer	12	12	3	4	71%	100%	27%	36%
	Lilly	3	1	3	1	19%	33%	100%	33%
	Bayer	2	0	0	2	13%	0%	0%	100%
	All	17	13	6	7	100%	75%	38%	44%
Process	Pfizer	7	7	1	2	54%	100%	14%	29%
	Lilly	4	2	4	2	31%	50%	100%	50%
	Bayer	2	1	1	2	15%	50%	50%	100%
	All	13	10	6	6	100%	77%	46%	46%
Formulation/dosing	Pfizer	18	18	8	8	64%	100%	44%	44%
	Lilly	5	2	4	1	19%	40%	80%	20%
	Bayer	5	2	2	4	19%	40%	40%	80%
	All	28	22	14	13	100%	78%	48%	44%
Fixed dose combination	Pfizer	21	21	15	15	75%	100%	71%	71%
	Lilly	1	0	1	0	4%	0%	100%	0%
	Bayer	6	5	4	5	21%	83%	67%	83%
	All	28	26	20	20	100%	93%	71%	71%
Indication/use	Pfizer	35	35	19	18	61%	100%	54%	51%
	Lilly	9	3	8	2	16%	33%	89%	22%
	Bayer	13	7	6	12	23%	54%	46%	92%
	All	57	45	33	32	100%	79%	58%	56%

with PDE5 inhibitors, and none of the substance patents are relevant to this analysis. Pfizer is also the dominant applicant in the other patent categories, having comparably high shares of formulation/dosing, fixed-dose combination, and use patents. Lilly, in contrast, shows a rather moderate patenting behavior, while Bayer appears to be relatively aggressive in these categories as well. So the latter three patent categories, which were, in general, filed relatively late in the lifecycle, may be used to a high degree for offensive blocking purposes. *Defensive* blocking may have taken place primarily during the early stage of the lifecycles, since most substances mentioned in patents from various categories explicitly cover multiple molecules plus their salts, hydrates, or isomers, but only one of these molecules is actually approved. Therefore, many patents have the potential to fulfill offensive and defensive blocking as well as imitation protection purposes simultaneously.

5.3. Substitutive and complementary patents

Content analysis of the claims revealed that substances (and variants of them) are used in many independent claims jointly with process, formulation/dosing, combination, or use descriptions. This means that all these patents are technologically complementary to the basic substance patents and, hence, legal substitutes. For crystals, enantiomers, and other chemical modifications of the substance, formulation/dosing, and process patents the potential for economic substitutability is relatively high. However, after expiration of the basic substance patent, generic products may be introduced, and novel crystals, formulations, or processes may protect further developments of the once-approved drug. In contrast, fixed-dose combination and use patents seem to usually substantially narrow the area of application and thus, the market volume protected from generic entry.

6. A model of patent fencing in pharmaceuticals

The model derived from patenting activities in the field of PDE5 inhibitors is outlined in Table 5. It shows for each patent category how far the PDE5 patent filings may have been used to prevent imitation and block competitors, and which economic potential for

substitution is associated with these patent categories, differentiating between the early and late stage of the life cycle.

Within this model, pure substance patents were primarily filed in the early stage of the drug lifecycle. Here, when the drug is not yet approved on the market, it is important to prevent imitation of the substance. Imitation protection also means preventing substitution, which is, according to Barney (1997), a specific form of imitation, as long as the underlying technologies are very similar. Competitors may develop similar molecular forms that the patentee of the first-in-class drug may have overseen. Therefore, the substance patents filed to protect the drugs' active ingredient may serve imitation protection purposes, and these patents were incorporated into the FDA Orange Book. Substance patents are typically very broad, protecting multiple substances that are substitutive. However, isomers, crystals, and salts of the active ingredient of the drug can also be considered as substance patents. These, in contrast, have been filed throughout the lifecycle and may potentially represent important economic substitutes. In the early stage, such patents may serve defensive blocking purposes, keeping other original drug makers at distance, but when substituting the original substance during the later stage in the drug lifecycle, imitation protection should be the primary concern for filing such applications. Hence, if a patent is filed for

Table 5

Model for the early and late stage of patent lifecycle management of PDE5 inhibitors based on a basic substance drug patent as a baseline: strategies for filing additional patents according to category (crystals/isomers/etc., process, formulation/dosing, fixed-dose combinations, and use), function (imitation protection and blocking), and potential for economic substitutability (high/low).

Lifecycle stage	Early		Late	
	Imitation	Blocking	Imitation	Blocking
Crystals, isomers, etc.	High	High	High	
Process	High		High	
Formulation/dosing	High		High	High
Fixed dose combination			Low	Low
Indication/use			Low	Low

The late stage begins as soon as the first drug was introduced into the market. Blank spaces indicate low occurrence rates for related patent filings.

imitation protection or blocking purposes, these intents not only depend on the patents' content but also on the timing of its filing.

Process patents, which were also filed in the early stage, protect new manufacturing methods and go hand-in-hand not only with novel substances but also with formulations, separately protecting even intermediate products, which might be easier to defend in infringement cases than the exact replication of a process. Depending on the nature of the substances manufactured, process patents often enhance prior manufacturing processes, or they may even substitute prior processes. Economically, these patents may turn out to be technical substitutes of basic drug patents. They should primarily prevent imitation, as developing processes that are not established in-house is a tedious task, and finally they should address generic rather than original drug makers, because the latter might develop slightly different processes based on different steps in chemical synthesis with different intermediate products/molecules (Hutchins, 2003).

Formulation and dosing patents were filed throughout the lifecycle. They have the potential to add to, but also to replace the product program of a drug, and, as they may substitute for previously marketed versions of the drug, may unfold substantial economic substitutability. In the early stage of the lifecycle, they primarily may have aimed at preventing imitation, while later they usually covered competitors' substances (see, e.g., Table 4); hence, they additionally seemed to fulfill an offensive blocking function.

Fixed-dose combinations were filed during the later stage, offering complementary products that allow selling several drugs within a single pill. Such an approach may enable novel patent protection for the drug, significantly extending patent protection, albeit the specific market for such a combination may be smaller than for the indications marketed first. Combinations may have been filed both to prevent imitation of such products, but also offensively to block competitors from introducing such a combination using their own patented substances within a possible market niche, as may be observed in Table 4.

Indication patents were filed about in parallel to fixed-dose combination patents, with potentially a similar intent. Such filings should aim at preventing imitation in cases where, in fact, further indications of the substances are marketed. Especially in the later stage, they may also cover competitors' substances, fulfilling blocking purposes. Again, this might be important to appropriating revenues in niche markets, which competitors could not enter any more (hence, as fixed-dose combinations, having a smaller economic potential to substitute (multiple) drugs based on broad substance patents). While the introduction of generic drugs pushes original drugs into market niches still protected by patents, by the same token blocking brand-name competitors from such niches helps to maximize revenues from the remaining original product.

7. Discussion and conclusion

7.1. Implications for research

The model developed in this paper for the PDE5 patent filings complements previous research on different patent categories filed over time (Howard, 2007). It may also stimulate further research on motives for seeking patents including blocking and imitation protection (Blind et al., 2006), but also using patents that constitute economic substitutes to prolong value appropriation. To date, separate research streams on such drug lifecycle management and patent fencing activities have lacked a common understanding of how these activities interact, for which the model developed in this paper offers some explanations.

The analysis and model derived in this paper show that fencing often comprised filing technologically complementary patents,

which also involved filing patents with the potential to offensively block competitors, with differing potential to economically substitute prior drug patents. I also derive that patents with extensive offensive blocking potential were predominantly filed in the later stage of drug lifecycle management, when the exact substances claimed by competitors are known in the industry, while patents with defensive blocking potential could primarily be found before, mirrored by filing multiple, related substances.

7.2. Managerial implications

This paper acknowledges that patents are not alike, and that the effectiveness of patenting depends on routines, skills, and strategies. However, it does not follow the recent literature on organizational structure and processes behind patent filings, such as the work from Somaya et al. (2007) or Reitzig and Puranam (2009). Somaya et al. (2007), for instance, studied the effect of in-house patent departments and knowledge about patenting on the patenting output of Fortune 500 firms. Reitzig and Puranam (2009) looked at organizational cross-functionality in patent management, product development teams, and patent grant success. Instead, this paper follows the approach from Sternitzke (2009) who studied filing routes and the speed at which patents are granted; this study focused on filing patterns that are not necessarily tight to organizational aspects, but rely on patent legislation and skills in using the patent system with maximal effectiveness.

The model derived in this paper goes beyond this body of literature, explaining when certain types and categories of patents may have been filed for PDE5 inhibitors to create patent fences and enhance value appropriation, expanding prior findings from the organizational literature by examining in detail how patent applications have been drafted. Because the strategies described here may create highly effective ways to extend patent terms for products and thus help keep product prices high, they may stimulate IP and product development strategies for a range of brand-name pharmaceutical companies. They may, however, also attract the attention of generic drug makers, who could pre-empt such strategies with, for example, defensive publishing, making it difficult for drug makers to market line extensions later on.

The model outlined in this paper is based very much on the specific regulatory environment for pharmaceuticals, where patent expiration leads to drastic reduction in brand-name sales because of generic competition. Nevertheless, parts of the patenting strategy may be also relevant for other industries. The closest one, which does not require further elaboration, is the chemical industry. But material science or electronics also may benefit from such a model. Taking electronics as an example, let us take as a hypothetical example a basic patent that relates to a novel design of a transistor with superior characteristics, based on both the use of novel material as well as on a specific arrangement of parts contributing to the basic transistor's functionality. Technologically substitutive patents would involve different materials, or different designs, or new processes describing alternative means to deposit thin layers of semiconducting material. In this light, novel combinations of several electronic components (for example, those that reduce the wattage of the system) may be comparable to fixed-dose combinations. New layouts or dopants for creating such transistors would be comparable to dosing/formulation patents, and adjusting electronic properties of the transistor might open up novel applications, such as in high-frequency circuits, and they would be technologically complementary and economically substitutes. These different inventions might be filed both for imitation protection and for blocking purposes. However, the incentives to file such additional patents in electronics at the end of the basic patents'

term are lower than in the pharmaceutical industry, with its high level of regulation and its much longer product lifecycles.

7.3. Limitations and future research

There are a number of limitations of this paper. First, as a case study, it relates exclusively to one class of drugs, PDE5 inhibitors, which may show some unique properties. Second, during data assembly, I found two patent families from Pfizer and Bayer that could fall under the legal scope of the vardenafil basic patent, but they were not classified accordingly by Chemical Abstracts. This means that even more chemical patents may be out there, implying that the patent data presented in this paper represent the lower boundary of the mutually blocking patenting activities we can expect. Third, the estimations of offensive blocking as measured by classifications of the CAS database are at the lower boundary of occurrences. The reason is that the manual inspection of claims revealed some patents broadly claiming PDE5 inhibitors in the independent claim, while dependent claims further specified the PDE5 inhibitors as vardenafil. CAS regarded such patents as covering solely vardenafil, rather than considering all PDE5 inhibitors. Fourth, even though some patents have a strong potential to fulfill imitation or blocking functions, they could have been filed with different motivations.

Future research could study other classes of drugs as well and deductively test the model developed in this paper. Such work might also address potential boundary conditions of the model, including time differences between introducing the first-in-class drug and follow-on drugs, and also different development times of these products. In addition, the number of competitors as well as drug characteristics that are perceived as benefits from the customers' perspective might influence patenting activity of the players, as might their market power. Future research could also integrate data on R&D and product strategies into the analysis, which might complement the views on patenting strategies and link them to organizational theory. Finally, it could also be worthwhile to study the effect of patent expiration, and what categories of patents are filed shortly before such events to prevent imitation by generic manufacturers.

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