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Patent race-like competition in drug lifecycle management

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Abstract

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In patent races, competing firms conduct R&D and file patents in order to hinder market entry by competitors. Despite a vast body of theoretical work on patent races, there is a lack of empirical evidence. This paper makes a first attempt to identify patent races in pharmaceuticals. The dataset relies on drug lifecycle management activities within a class of drugs where firms strive to expand patent protection into niche markets by filing additional indications for their substances. Therefore, the competitive dynamics of filing such additional indications were studied. Although some cases could be found where firms were neck-and-neck (as proposed in the theoretical literature), the patents coming first did not prevent granting of the later patents. The results contribute to both the literature on patent races, entry barriers, and optimal patent breadth.

Keywords: pharmaceuticals, patent races, entry barriers, competition, preemptive activities

1. Introduction

There is a long tradition of research on market structure, strategic interaction, and R&D (Schumpeter 1934, 1942), which also has resulted in a vast body of economic literature on technology or R&D races, which are frequently assumed to be patent races. Basically, it is assumed that at least two competitors are investing in R&D to come up with a new product. In order to appropriate the returns from their investment, prevent market entry of their competitors, and achieve a dominant position in the market, they file a patent (e.g., Loury 1979; Lee and Wilde 1980; Harris and Vickers 1985a, 1985b). Strategy and entrepreneurship scholars have seen patent races as one source of first-mover advantages of firms (Lieberman and Montgomery 1988; Deeds and Hill 1996), while such pioneering businesses frequently dominate a market (Kerin et al. 1992; Golder and Tellis 1993). The pharmaceutical industry, where patents play an important role to prevent imitation (Mansfield 1986), is assumed to be a hotbed for patent races (Deeds and Hill 1996; Lieberman and Montgomery 1988; Malerba and Orsenigo 2002).

Prior work in the industrial organization literature has developed an extensive set of game-theoretical patent race models, which make different assumptions about the competitive setting of the firms, such as the starting points of the race, spillovers, etc. Much of the work done in this field, which is growing with accelerating pace¹, has been criticized as being “highly stylized and counterfactual” (Cohen and Levin 1989). In fact, empirical work that actually supports the extant theoretical papers in this field is sparse (Hur 2010; Doraszelski 2003; Cohen and Ishii 2006). To date, it has been looked more on competitive actions on the product or firm level (Cockburn and Henderson 1994; Lerner 1997; Czarnitzki and Kraft 2004; Khanna 1995), while there are only two empirical studies that have studied patent race-like behavior before: Schroth and Szalay (2010) study financial constraints in patent races, but

¹ A search for articles on patent races within the Social Science Citation Index revealed that, since the 1980s, the amount of publications has doubled every decade.

their measure of race situations is rather stylized, as will be discussed below, raising doubts about the validity of their results with respect to the patent race literature. Cohen and Ishii (2006), who nicely tackled the problem of identifying races in a cross-industry sample, find extremely low rates of race-like situations. In addition, Cockburn and Henderson (1994) present two important points in their study of the pharmaceutical industry. First, managers in this industry deny the existence of patent races, and second, they can show that, within a class of drugs, followers introduce substances which are similar than those of the pioneer. The latter behavior seems to be the rule rather than the exception (DiMasi and Faden 2011).

These observations raise two important questions: First, is the still increasing research done on patent races addressing rare events? Second, how far does patenting through races by pioneers prevent competitive entry? The latter point is also of relevance for the literature on entry barriers (see e.g. Smiley 1988; Demsetz 1982). Further, it raises questions on the role of patents for obtaining pioneer positions (Lieberman and Montgomery 1988), and it addresses economic research on patent breadth (see e.g. Gallini (1992) or Denicolo (1996)).

This paper explores race-like behavior in the pharmaceutical industry in order to answer these research questions, while providing a method to reliably identify patent races (which seems to have been a major challenge in the past). Instead of studying the introduction of novel substances within classes of drugs, it looks at activities stemming from drug lifecycle management activities where firms aim at extending exclusivity for their drugs as long as possible (Gorlin 2008; Howard 2007). In this context, firms strive to identify more indications for their once-approved substances (Sandner and Ziegelbauer 2008). Hence, it is likely to observe racing behavior in this setting. Therefore, in this paper, patent activity within a class of drugs was studied, observing three firms that each brought drugs onto the market and which all filed a substantial number of additional patents relating to the same substances (Sternitzke 2013). The content of the patents' claims was studied in detail, eliciting words

from the patent claims in order to assess for which indications the substances contained therein were supposed to be used, i.e. which diseases might be treated with the substances claimed within the patents. The filing patterns of the corresponding patents were tracked over time, jointly with analyzing data from selected examination reports to uncover how far later patents cited earlier ones for novelty-destroying purposes.

As a result, no races could be identified where the outcome was a patent that successfully hindered followers to also patent their work (which is implicitly assumed in the patent race literature), implying that such activities appear to be relatively rare events, while these patents barely present entry barriers. The reason is that patents have rather narrow claims that allow competitors bypass parallel inventions.

The paper is organized as follows. The second section presents the prior work on patent races. Data and methodologies are explained in section 3, results are presented in section 4. Discussions and conclusions follow.

2. Theory

2.1 Patent race models

Race models try to describe organizational behavior and its boundary conditions in competitive situations. Reinganum (1989) provides an excellent overview about the early literature in this field, which can be mainly differentiated into symmetric and asymmetric models. In symmetric models, it is assumed that at least two firms start racing for a patent at the same starting line, whereas in many cases only one firm obtains the patent (which is referred to as a winner-takes-it-all situation or as an indivisible price). This patent then serves as an entry barrier in the market, while the firm obtains superior rents. Examples for such race models are the work of Dasgupta and Stiglitz (1980), Lee and Wilde (1980), or Loury (1979). In contrast, in asymmetric races there are different starting lines for the competitors.

Typically, situations of incumbent/monopolist and followers/new entrants are discussed, describing situations of preemptive patenting. Examples for work on asymmetric patent races are Fudenberg et al. (1983), Gilbert and Newbery (1982), Harris and Vickers (1985b), or Reinganum (1983, 1985). Zizzo distinguishes the prior literature into models based on technological uncertainty, dynamic uncertainty, or both (Zizzo 2002). Technological uncertainty refers to stochastic outcomes of the race, an assumption contained in the models from Dasgupta and Stiglitz (1980), Lee and Wilde (1980), or Loury (1979). When incorporating dynamic uncertainty into their models, scholars accounted for changes in the information base the parties in the race obtain over time, such as knowledge on success or failure of their competitors Gilbert and Newbery (1982), but also spillovers (D'Aspremont Jacquemin 1988; De Fraja 1993)). Many scholars also assume complete information about competitive activities here (Harris and Vickers 1985a, 1985b). Models that include both technological and dynamic uncertainty have also been presented Grossman and Shapiro (1987) and Harris and Vickers (1987).

Over the course of time, patent race-like situations have been used to explain, among others, preemptive patenting (Gilbert and Newbery 1982), public R&D policy, especially with respect to subsidies (Beath et al. 1989), patent output based on financial characteristics of firms (Meng 2008), patenting versus secrecy (Bulut and Moschini 2006; Schneider 2008), and strategic disclosure of information (Baker and Mezzetti 2005; De Fraja 1993).

All these papers describe how patent races occur from a theoretical point of view, they frequently rely on a narrow set of assumptions that are both unstable with respect to minor changes in the information structure Cockburn and Henderson (1994), they have been described as “highly stylized and counterfactual” Cohen and Levin (1989), and they hardly meet patenting practice: Especially symmetric situations where firms have very similar starting situations should be rare in practice. Firms also face both technological and dynamic

uncertainty, they benefit from spillovers, and they may patent preemptively at the same time. But not enough, there are various motives and ways to file different types of patents, depending on the situation and industry (Blind et al. 2006; Cohen et al. 2000; Sternitzke 2013).

Despite the numerous theoretical studies on R&D and patent races, there is little empirical evidence for these phenomena (see also Cohen and Ishii 2006; Doraszelski 2003; Hur 2010). Some work has looked at R&D races without explicitly discussing the role of patents therein: Czarnitzki and Kraft (2004) studied R&D spending of leaders and followers using a cross-industry sample. Khanna (1995) looked at racing in three areas of the computer industry, showing that firms conducted larger jumps in performance when lagging technologically, explaining this phenomenon with switching costs and spillovers. Lerner (1997) showed that the propensity of disc drive manufacturers to innovate depends on their technological position, confirming the results from Khanna (1995). There are also two studies focusing on the pharmaceutical industry: Berndt et al. (2003) and Cockburn and Henderson (1994) studied the introduction of novel substances within a class of drugs each (as will be described below).

Only two papers could be identified that explicitly studied patent race-like behavior. Schroth and Szalay (2010) looked at patenting of US firms, attempting to show that financial means have a positive impact on winning a race, which is frequently assumed in the theoretical literature (see e.g. De Fraja 1993). More specifically, Schroth and Szalay (2010) assume that all those firms participated in a race which patents' have been the most highly cited in the race-winning patent. Given the coarse nature of US patent citations (Michel and Bettels 2001), one must be very cautious in assuming that firms which have been highly cited were also working on filing the same invention. The overall results of their work may as well be explained with the fact that the propensity to patent increases with firm size (Mansfield

1986), as the cash position of firms usually does, while the authors did not control for firm size in addition to the firms' cash position.

In their working paper, Cohen and Ishii (2006) study patent races and the role of incumbents to delay information therein. In contrast to the study from Schroth and Szalay (2010), they found an elegant solution to identify patent races, deriving race-like situations from US patent interference cases. Such cases originate in the first-to-invent system where the date of the invention, not the filing date as in many other jurisdictions, is relevant for assigning priority to an invention. In the US, applicants have a period of 12 months after the date of the invention to file a patent on the invention. In cases where two parties have filed patents closely to each other and only one patent would get granted by the patent office, an interference procedure may clarify who was actually first and, therefore, will receive the patent. The authors study US court files and found that only 1,400 cases occurred between 1988 and 1994. Given the about 795,000 patents applied for during this period, such patent races seem to exist in well below one percent of all cases.² However, there might also exist race situations which might not be captured by interference cases. For pharmaceuticals, Sternitzke (2009) has shown that firms tend to file their patents in much more countries than applicants from other industries. But in order to do so, they have to rely on the internationally dominating first-to-file rule and not the first-to-invent principle which is almost unique to the US. Thus, it may be dangerous to postpone patent filings here, contrary to firms being active in industries with a much higher focus on the United States where postponing a filing might be less critical under the light of interference cases.

² Kingston (2004) confirms this ratio of interference cases and finds that pharmaceutical patents are the patent class with the highest incidence rate.

2.2 Racing in pharmaceuticals?

Deeds and Hill (1996), Lieberman and Montgomery (1988), and Malerba and Orsenigo (2002) mention that competition within pharmaceuticals follows the patterns of patent races. Patent protection is particularly strong here. The propensity to patent is relatively high Arundel and Kabla (1998), and patents can be seen as a prerequisite as, without patent protection, pharmaceutical drug development, which is extremely costly, would certainly not be undertaken Mansfield (1986). Approved drugs which are protected by one or a few patents may be significant sources of multi-million to multi-billion dollars of annual revenues. Therefore, even short lead-time advantages may be highly profitable in pharmaceuticals. In this context, firms typically file substance patents when identifying a novel drug Sternitzke (2013). These substance patents are legally very broad, as they prevent others from using the substance in any context. However, when patent rights in pharmaceuticals expire, the patent holders face generic entry and strong declines in sales Raasch (2006). Hence, the incentives are high to not only being first-to-market and keep competitors out of the business as long as possible. Also maximizing revenues of once-introduced drugs can frequently be encountered, extending patent life of the products which has become known as drug lifecycle management.

There are at least two important ways to block competitors in pharmaceuticals: (i) occupying a novel class of drugs (i.e. families of molecules that address a specific biochemical process in the human body), or (ii), within such a class of drugs, protecting specific indications (e.g. certain dysfunctions which can be treated with molecules from that drug class) in the context of drug lifecycle management.

Regarding (i), usually there are multiple drugs within a class, as several studies have shown (Berndt et al. (2003), Cockburn and Henderson (1994)), looking at competition on the product (and substance) level, without explicitly analyzing effects of patenting. Both could show that follower products had fewer side effects and that the first two drugs dominated the

market with a combined market share above 70 percent. DiMasi and Faden (2011) described the tendency of pharmaceutical firms to develop more than a drug per class as race-like. They could show that between the first drug within the class and follow-on products, which typically comprise different molecular structures for the same mechanism of action, the time interval has decreased significantly during the last decades, from about 14 years for drug classes having emerged in the 1960s to less than three years in the 1990s. Giving such long time intervals between product introductions, it can be assumed that competitors already benefitted from spillovers of the leader, as their patent applications are typically published within 18 months.³ However, it is debatable if the time intervals described by DiMasi and Faden (2011) can, in fact, still allow speaking of a race here, as Harris Vickers (1985b), p. 206 denotes: “Once a player is “far enough ahead” in the race, it ceases to be a real contest.” The findings from DiMasi and Faden (2011), but also from Berndt et al. (2003), or Cockburn and Henderson (1994) further illustrate that obviously multiple patents per class are very common, implying that winner-takes-it-all effects are rather rare, while only the first few drugs have a chance of being commercially successful.

Apart from patenting novel substances within a class of drugs (i), there are patenting effects regarding drug lifecycle management activities (ii). In order to still appropriate rents from their R&D once generic manufacturers enter the stage, firms aim at extending the patent protection stemming from the original substance patents by filing multiple patents on product improvements over the course of time. These allow extending the original patent protection by a couple of years based on novel formulations, dosing, or line extensions addressing novel indications, even after expiry of the basic substance patent (Gorlin 2008; Howard 2007; Sternitzke 2013). Sandner and Ziegelbauer (2008) mention that 84 percent of all drugs sold in

³ For a long time, US patents were only published at the time when granted, which usually takes longer than 18 months. However, in pharmaceuticals most drug patents are filed internationally, meaning that corresponding patent applications had been available after 18 months via the patent offices abroad.

the United States were addressing more than one indication, while an additional 6 percent had novel indications under development. Such novel indications may open up market niches for the original substance and generate substantial revenues. Sternitzke (2013) discovered that firms, when patenting novel indications, also claimed their competitors' substances at the same time, which may block them from entering these markets. This may be an attractive strategy when the niches are small, and occupying such niches early, maybe via a race, enhances appropriability. Furthermore, once a drug maker has also occupied a niche while blocking it via patent claims covering also its competitors' substances, inventing around specific substances becomes much more costly. This may imply that such drug lifecycle management effects may much more effectively preempt competitive entry as in the case of competition on new substances inside newly established drug classes as discussed above.

Therefore, this exploratory paper seeks to clarify the situation by searching for race-like behavior inside a drug class regarding filings for novel indications as one form of drug lifecycle management.

3. Methodology, field of research, and data

3.1 Identifying races

The approach to identifying patent races is based on both the notion that competitors must be close so that there is 'a real contest' (Harris and Vickers (1985b), p. 206) and a limited base of information about the progress of the competitors. These two points can be fulfilled when looking at situations where patents on the same indications were filed within a period of 1.5 years, using the peculiarity of the patent system that applications are laid open after 18 months. The dynamics are then the following: Let's take company A as an example. It files patent x at $t=t_0$. Company B files a patent y at $t=t_0+16$ month on the same indication. At this point in time, company B could not be aware of patent x as it was not laid open yet. In contrast, company C may also be interested in the field and doing research therein, but

lagging behind. It may be preparing a patent filing about 19 months after company A, but, by monitoring the patent activity of its competitors, would then find out about the filing of patent x. Company C may then back away from filing its patent as it learns from the information available in the market that the niche it was targeting is already occupied. One could also argue that company C was too far away from company A in order to speak of a patent race going on here. Successful entry deterrence then is assumed when the patents of the laggards are not granted due to the prior filing of the race-winners, as indicated by citations in examination reports. These older patents would then anticipate the novelty of the invention.

3.2 Field of research

This paper studies patenting activities within the class of PDE5-inhibitors (phosphodiesterase type 5-inhibitors), a class of drugs that moderates smooth muscle relaxation and leading to vasodilation (widening of arteries) by blocking a substance called cyclic guanosine monophosphate (cGMP). Several companies were striving to use cGMP-blockers to treat patients with angina pectoris or hypertension. The first substance was synthesized at Pfizer Ltd. in England, known as sildenafil and marketed under the brand Viagra. Later, Lilly and Bayer also introduced substances such as tadalafil (Cialis) and vardenafil (Levitra). Contrary to prior expectations, the first commercial use of these drugs was treating male erectile dysfunction, with pulmonary hypertension following later (brands here are Revatio for sildenafil and Adcirca for tadalafil). The discovery of the first-in-class drug is described in Katzenstein and Grossman (2001) or Trott (2008). Since then, various other uses have been found Dorsey et al. (2010).

3.3 Data

The dataset is related to one by the same author and assembled for some other work on patenting in pharmaceuticals, relying on secondary data sources (ANONYMIZED). In brief, PDE5-inhibitors were identified via a recent article Dorsey et al. (2010), and only those were

considered that had been approved in the United States by 2011. These substances were searched in the Chemical Abstracts (CA) database using the CAS-number, a unique ID that is used by CAS to track e.g. all patents published that mention the substances. In order to elicit which content was actually claimed (unbiased by examination results), the analyses are primarily based on patent applications, not necessarily granted patents.

The results from the search in the CAS database were transferred to the Minesoft PATBASE database to elicit which of the patents found belong to the same patent family.⁴ From there, the data were transferred to a spreadsheet program for further processing: Manual data cleaning took place, eliminating patents that, e.g., mentioned these substances coincidentally and were, therefore, not considered to be part of lifecycle management activities. The families which were identified also contained multiple US patents stemming from so-called continuation applications. Continuations allow splitting up a patent document, or they allow adding novel matter that has emerged over the course of time (see, e.g., Lemley and Moore 2004; Hegde et al. 2009). Patent claims were investigated in more detail for each published US patent document and the first patent document of a patent family (either an application at the European Patent Office (EPO) or via the Patent Cooperation Treaty (PCT)). Here, the content of the claims was studied manually to elicit patents targeting specific indications, but also to identify if the patent was a substance patent, or one focusing on novel dosing/formulation, the combination of drugs, or even processes. In total, 72 patent families with 137 patent documents were detected, stemming from Pfizer, Lilly, and Bayer. This dataset was subsequently narrowed to those comprising indications, yielding 58 patent families. In addition to the prior-mentioned steps, examination reports from the US Patent and Trademark Office's Pacer system were studied for the selected documents to elicit references made by examiners from later applications to earlier ones in order to challenge the novelty of

⁴ A patent family refers to all patents that were filed for the same invention.

the invention, i.e. to uncover that the later patents were not granted and the winner of the race obtained the patent. So far, using the Pacer system represents a novel data source in patent-related research.⁵

In order to further investigate indications mentioned within the patent documents, the indications found were manually structured according to the hierarchical MeSH classification (Medical Subject Headings, a controlled thesaurus provided by the US National Library of Medicine). The MeSH thesaurus provides not only alternative terms/synonyms for identical indications. Due to its hierarchical structure, it also allows to assess if the terms used refer to a more general or a narrower description of the indications (i.e. narrower or broader categories, such as cardiovascular diseases in contrast to its sub-category heart failure). By doing so, it was not only assured that patent applicants could not hide specific indications from searches done by competitors.⁶ Taking such hierarchy into account is also important for assessing the novelty of an indication. For instance, when treatment of diseases has been claimed on a superior level, it is unlikely that, later, a disease on a lower level can be still claimed successfully. However, this must not be the case the other way round, as higher level diseases may involve much more mechanisms being relevant for a disease.

4. Results

Tables 1 and 2 provide insights into the amount of different indications claimed in the 58 patent families that all comprised at least one indication. Synonyms of indications were summarized with one term, and indications from different hierarchical levels were counted independently. In total, about 180 different indications were mentioned in the dataset (see Table 1). On average, there are about six indications in every US patent document (which

⁵ As long as a patent is not granted (as postulated implicitly in winner-takes-it-all races), references made by examiners only appear in examination reports available via the Pacer system.

⁶ Manual inspection of the claims could rule out the possibility that the applicants were able to hide specific indications through choosing unusual wording.

have at least one indication). Two patent families (i.e. #2 from Lilly) and #45 (Pfizer) have more than 40 indications, with the maximum amount for #55 (Pfizer) and #61 (Bayer) with 53 and 54 indications, respectively.⁷ This raises doubts if all these indications have proven interactions with the substances claimed, appearing more like guesses of potential relationships.

{insert Tables 1 & 2 about here}

On average, each indication is mentioned in about 2.5 patent families (see Table 2), and the indication mentioned most frequently is female sexual dysfunction (18 families), erectile dysfunction (17 families, but there is still a higher level term “male sexual dysfunction” mentioned in five other patent families), hypertension and cardiac insufficiency (12 families each), followed by pulmonary hypertension with 11 families. These numbers reflect the high level of research activities for drugs such as Revatio and Adcirca which have been approved based on the same chemical substances for treating pulmonary hypertension, and finding some kind of “Viagra for females”.

Figure 1 reveals that Pfizer aimed at protecting the largest amount of different indications with its patents filed for PDE5 inhibitors, namely 117, followed by Bayer with 77 and Lilly with 51.⁸ Only 13 were tried to be patented by all three applicants. The overlap between Bayer and Lilly is relatively small; each of them seems to focus on rather different areas. The overlaps between Pfizer and Bayer and Pfizer and Lilly are about similar in size. Pfizer filed the largest amount of indications not covered by its competitors as well, followed by Bayer, with Lilly going towards “own” indications only sparsely. This picture underlines that Pfizer as first-in-class patentee aims to protect its R&D base far more broadly than the other two firms, while Lilly is following a very selective strategy.

⁷ The numbering indicates the order in which the families were filed.

⁸ These include also higher-level descriptions according to the MeSH thesaurus.

{insert Figure 1 about here}

In a first step, the 13 indications mentioned by all three competitors were studied in detail, indicating a particular interest in the field, and their filing patterns are illustrated in Figure 2. Further, the remaining 37 were analyzed which were claimed by only two of the three competitors (without graphical illustration).

Figure 2, therefore, shows patent filings chronologically based on their priority date. Indications on a higher hierarchical MeSH level are also listed. White circles relate to filings by Lilly, light grey ones to Pfizer, and dark grey ones to Bayer. Patent families are numbered in the order of priority, excluding those that did not contain any indications. Continuation applications are shown when they contained different indications than in the prior applications. The type of continuation is defined via the shape of the rims.⁹ Thick rims indicate granted patents. In total, there are five main categories of indications, namely cardiovascular diseases, asthma, the urinary system, the genital system, and depression:

Cardiovascular diseases, asthma: These two areas are dominated by the first patent from family #4. So the indication was claimed first for a PDE5 inhibitor several years earlier than many of the remaining patent filings, which certainly does not allow protecting other known PDE5 inhibitors with this indication without adding another novel, nonobvious component to that patent application. Therefore, no further inspection took place in this area.

The urinary system: In the area of lower urinary tract syndrome (LUTS) indications, Lilly filed the treatment of benign prostate hyperplasia (BPH) as first indication in 1998. This patent was also granted. Then, Bayer started filing for bladder disorders and incontinence (July 23, 2001), shortly followed by Pfizer (December 6, 2001), which claimed LUTS in general. So Bayer and Pfizer may have been in a race for broader applications of PDE5 in this

⁹ It is differentiated between continuation applications (CAP), continuation-in-part applications (CIP), and divisional applications (DIV). CAPs rely on the same content claimed in the first application of the patent family, while CIPs, in contrast to CAPs, refer to novel content added at a later point in time.

field. The Bayer patents were granted, not the one from Pfizer which related to both dosing and uses. Interestingly, one of the granted Bayer patents is a continuation, referring back with one priority date before the Lilly patent claimed BPH.

Genital system: In the area of sexual dysfunction, erectile sexual dysfunction was mentioned as first indication, mentioned in a 1993 patent. Pfizer started adding female sexual dysfunction with its filing on December 16, 1997. Lilly followed with its first application claiming the same subject on April 30, 1999, six weeks before the first patent document from Pfizer was published. So Pfizer and Lilly might have been in a race here as well. While none of the early Pfizer patents were granted, Lilly obtained patent protection for this indication. For premature labor, the time distances were too large in order to be able to speak of a race here.

Depression: Here, Lilly as the first filer (Jan 28, 2003, published Oct 5, 2006), claiming all three substances. Pfizer was a follower only six weeks later, filing a patent on a novel substance, dosing, combination, and use, but also Bayer (August 6, 2004) with a pure use patent. So eventually, there might have been a race here, too. None of these patents was finally granted.

{insert Figure 2 about here }

From these findings one would speculate that the reason why many the later patents were not granted was the filing the novel indications earlier. In order to verify this, the examination reports for these patents were studied (where available). In none of the cases the particular indications mentioned above played any role in granting the patents. Other aspects such as the substances (or sub-forms of them), dosing or formulations, etc. were much more important in the decision to grant the patents.

In addition to the 13 indications claimed by all three competitors, the 37 indications were analyzed where there were at least two companies applying for. For five patents, filings

between the first and second patent mentioning the same indication occurred within the timeframe of 1.5 years, i.e. during the period when the first filing was not disclosed yet. They covered indications such as autoimmune diseases, neuropathy, cancer, epilepsy, and fibrosis. Except for the last indication, which included also novel substances, none of the applications was granted. In most of these cases examination reports were available, showing that the indications mentioned in the earlier patents from the faster players did not play a role for the granting decision of the later patents.

5. Discussion and conclusion

For the field of PDE5 inhibitors and its three main competitors it was investigated how far patent race-like effects could be observed regarding novel indications, which are frequently claimed in the context of drug lifecycle management. In total, 58 patents comprised indications, from which 52 contained indications claimed at least by two competitors. Searching for events where two competitors filed patents within a period of 1.5 years, during which they could not see if their competitors had filed any similar patents, eight such events were identified. In none of the cases, the earlier patents blocked granting of the later ones.

Despite of the favorable environment for patent races in pharmaceuticals, prior work had shown that, when racing for novel substances, often several competitors may obtain valuable patents (see, e.g., DiMasi and Faden 2011; Berndt et al. 2003; Cockburn and Henderson 1994). But also later during lifecycle management activities, even in the light of an intense patent activity as demonstrated by Pfizer as the first-in-class patentee, including intense blocking and the like (Sternitzke, 2013), firms cannot prevent others from introducing novel drugs and novel indications. The reason for successful new entry of competitors inside novel classes of drugs obviously lies in the complex nature of pharmaceutical mechanisms of action, which allow multiple, somewhat related molecules to perform key functions here. So when searching for novel molecules, firms may be successful even if competitors already

claimed some of them. For claiming e.g. novel indications inside the class of drugs, the study of the examination reports in this paper revealed that patentees often rely on different formulation or dosing, and hence, an heterogeneous resource base, which allows for novel patents. Therefore, the patent system does not seem to provide insurmountable barriers to competitors as assumed in the patent race literature.

First, this seems to confirm that patent races with successful entry deterrence by the leader are rather rare events, which is in line with the findings from Cohen and Ishii (2006) or Kingston (2004). Second, these findings lead to implications for the literature on entry barriers, which originate from reputational effects (Krouse 1984), advertising (Demsetz 1982), scale effects (Rao and Rutenberg 1979; Scherer 1975), learning curve effects (Smiley and Ravid 1983), or long-term contracts (Smiley 1988). Patents proposed from winner-takes-it-all situations are seen in a similar vein. But they hardly deter entry of new players, simply as the breadth of a single patent usually is too narrow. When Lieberman and Montgomery (1988) discussed the role of patent races for first-mover advantages, they referred to the asymmetric model from Gilbert and Newbery (1982), which centered on the effects of preemptive patenting. The authors underline their arguments referring back to Bresnahan (1985) with his work on Xerox and its dominant market position protected by a large patent portfolio, as well as Bright (1949) who described how Edison acquired important patents around his basic one on the electric light-bulb, a strategy which resulted in a strong pioneering position. So entry deterrence appears to be the consequence of preemptive patenting, i.e. the filing of multiple, rather than a single patent, whereas preemptive patenting is not necessarily the consequence of an actual race. For instance, Sternitzke (2013) has shown that firms employ different ways to block competitors based on the way how they drafted their patent claims. Hence, first-mover positions may emerge from preemptive patenting, but they seem to rarely be the consequence of a patent race.

The findings from this paper that single patents hardly deter entry of new players may also have some implications on the literature stream on optimal patent breadth (see, e.g. Gallini 1992; O'Donoghue 1998; Barton 1996), where scholars are often concerned that overly broad patents hinder innovation. At least in the setting shown in this paper, overly broad patents do not seem to be an issue. Going further, and reconciling that entry deterrence appears to depend on preemptive activities, overly broad patent protection seems to stem rather from patent portfolios, i.e. bundles of multiple intellectual property rights.

The findings presented in this work are subject to some limitations. First, one could argue that the time-window of 18 months chosen in this study may be too narrow for the drug industry, which relies on clinical studies and animal models to identify mechanisms of action. However, the nature and amount of studies one needs to undertake remains the same for all players in the market (and they are subject to the firms' resources). In this light: Can we still speak of a race as it is commonly understood in the literature when the time period between the players is much longer (see Harris and Vickers 1985b)? Second, the dataset under investigation involved solely one class of drugs, only 76 possible combinations of indications¹⁰, filed via 58 patent families and only 8 situations where competitive patenting activity could be observed within the time window of 1.5 years. So, future research might see this work as a starting point and use large-scale studies that involve multiple classes of drugs or even other technological fields to help shed more light on the effects of patent races in practice. But, combining the results presented in this paper with those from Cohen and Ishii (2006) that find patent races to occur in only a very small amount of cases, it seems unlikely that such future work will show that patent races are a wide-spread phenomenon in practice, questioning the effort such an endeavor would require. Future research may, therefore,

¹⁰ 13 indications claimed by all three competitors plus 37 indications claimed by only two.

address rather different strategies how firms successfully preempt competition without actually racing.

References

- Arundel, A., Kabla, I., 1998. What percentage of innovations are patented?: Empirical estimates for European firms. *Research Policy*, 27 (2), 127-141.
- ANONYMIZED – available to the conference organizers upon request.
- Baker, S., Mezzetti, C., 2005. Disclosure as a Strategy in the Patent Race. *Journal of Law and Economics*, 48 (1), 173-194.
- Barton, J. H., 1996. Patents and antitrust: a rethinking in light of patent breadth and sequential innovation. *Antitrust Law Journal*, 65 449.
- Beath, J., Katsoulacos, Y., Ulph, D., 1989. Strategic R & D Policy. *The Economic Journal*, 99 (395), 74-83.
- Berndt, E. R., Pindyck, R. S., Azoulay, P., 2003. Consumption externalities and diffusion in pharmaceutical markets: antiulcer drugs. *The Journal of Industrial Economics*, 51 (2), 243-270.
- Blind, K., Edler, J., Frietsch, R., Schmoch, U., 2006. Motives to patent: Empirical evidence from Germany. *Research Policy*, 35 (5), 655-672.
- Bresnahan, T. F., 1985. Post-entry competition in the plain paper copier market. *The American Economic Review*, 75 (2), 15-19.
- Bright, A. A., 1949. *The electric-lamp industry*, Macmillan.
- Bulut, H., Moschini, G., 2006. Patents, trade secrets and the correlation among R & D projects. *Economics Letters*, 91 (1), 131-137.
- Cockburn, I., Henderson, R., 1994. Racing to invest? The dynamics of competition in ethical drug discovery. *Journal of Economics and Management Strategy*, 3 (3), 481-519.
- Cohen, L. R., Ishii, J., 2006. Competition, innovation and racing for priority at the US Patent and Trademark Office. *Law and Economics Working Paper Series*, University of Southern California Law School.

Cohen, W. M., Levin, R. C., 1989. Empirical studies of innovation and market structure. in: Schmalensee, R., Willig, R. D., The handbook of industrial organization, North Holland, New York, 1059-1107.

Cohen, W. M., Nelson, R. R., Walsh, J., 2000. Protecting Their Intellectual Assets: Appropriability Conditions and Why US Manufacturing Firms Patent (or Not). NBER Working paper No. 7552, <http://www.nber.org/papers/w7552>, (August 1, 2007).

Czarnitzki, D., Kraft, K., 2004. An empirical test of the asymmetric models on innovative activity: who invests more into R&D, the incumbent or the challenger? *Journal of Economic Behavior Organization*, 54 (2), 153-173.

D'Aspremont, C., Jacquemin, A., 1988. Cooperative and noncooperative R D in duopoly with spillovers. *The American Economic Review*, 78 (5), 1133-1137.

Dasgupta, P., Stiglitz, J., 1980. Uncertainty, industrial structure, and the speed of & D. *Bell Journal of Economics*, 1-28.

De Fraja, G., 1993. Strategic spillovers in patent races. *International Journal of Industrial Organization*, 11 (1), 139-146.

Deeds, D. L., Hill, C. W. L., 1996. Strategic alliances and the rate of new product development: an empirical study of entrepreneurial biotechnology firms. *Journal of Business Venturing*, 11 (1), 41-55.

Demsetz, H., 1982. Barriers to entry. *American Economic Review*, 72 (1), 47-57.

Denicolo, V., 1996. Patent races and optimal patent breadth and length. *Journal of Industrial Economics*, 44 (3), 249-265.

DiMasi, J. A., Faden, L. B., 2011. Competitiveness in follow-on drug R&D: a race or imitation? *Nature Reviews Drug Reviews*, 10 (1), 23-27.

Doraszelski, U., 2003. An R & D race with knowledge accumulation. *RAND Journal of Economics*, 34 (1), 20-42.

Dorsey, P., Keel, C., Klavens, M., Hellstrom, W. J. G., 2010. Phosphodiesterase type 5 (PDE5) inhibitors for the treatment of erectile dysfunction. *Expert Opinion on Pharmacotherapy*, 11 (7), 1109-1122.

Fudenberg, D., Gilbert, R., Stiglitz, J., Tirole, J., 1983. Preemption, leapfrogging and competition in patent races. *European Economic Review*, 22 (1), 3-31.

Gallini, N. T., 1992. Patent policy and costly imitation. *The Rand Journal of Economics*, 23 (1), 52-63.

Gilbert, R. J., Newbery, D. M. G., 1982. Preemptive patenting and the persistence of monopoly. *American Economic Review*, 72 (3), 514-526.

Golder, P. N., Tellis, G. J., 1993. Pioneer advantage: marketing logic or marketing legend? *Journal of Marketing Research*, 30 (2), 158-170.

Gorlin, D. I., 2008. Staving off Death: A Case Study of the Pharmaceutical Industry's Strategies to Protect Blockbuster Franchises. *Food and Drug Law Journal*, 63 823-864.

Grossman, G. M., Shapiro, C., 1987. Dynamic R & D competition. *Economic Journal*, 97 (386), 372-387.

Harris, C., Vickers, J., 1985a. Patent races and the persistence of monopoly. *Journal of Industrial Economics*, 33 (4), 461-481.

Harris, C., Vickers, J., 1985b. Perfect Equilibrium in a Model of a Race. *Review of Economic Studies*, 52 (2), 193.

Harris, C., Vickers, J., 1987. Racing with uncertainty. *Review of Economic Studies*, 54 (1), 1-21.

Hegde, D., Mowery, D. C., Graham, S. J. H., 2009. Pioneering Inventors or Thicket Builders: Which US Firms Use Continuations in Patenting? *Management Science*, 55 (7), 1214-1226.

Howard, L., 2007. Use of patents in drug lifecycle management. *Journal of Generic Medicines*, 4 (3), 230-236.

Hur, W., 2010. A multi-stage race model with strategic interaction: An agent-based simulation approach. *Technological Forecasting and Social Change*, 77 (4), 578-586.

Katzenstein, L., Grossman, E. B., 2001. *Viagra (sildenafil citrate): the remarkable story of the discovery and launch*, Medical Information Press.

Kerin, R. A., Varadarajan, P. R., Peterson, R. A., 1992. First-mover advantage: A synthesis, conceptual framework, and research propositions. *Journal of Marketing*, 56 (October), 33-52.

Khanna, T., 1995. Racing behavior - Technological evolution in the high-end computer industry. *Research Policy*, 24 (6), 933-958.

Kingston, W., 2004. Light on simultaneous invention from US Patent Office "interference" records. *World Patent Information*, 26 (3), 209-220.

- Krouse, C. G., 1984. Brand Name as a Barrier to Entry: The Rea Lemon Case. *Southern Economic Journal*, 51 (2), 495-502.
- Lee, T., Wilde, L. L., 1980. Market structure and innovation: A reformulation. *Quarterly Journal of Economics*, 94 (2), 429-436.
- Lemley, M. A., Moore, K. A., 2004. Ending Abuse of Patent Continuations. *Boston University Law Review*, 84 63.
- Lerner, J., 1997. An empirical exploration of a technology race. *Rand Journal of Economics*, 228-247.
- Lieberman, M. B., Montgomery, D. B., 1988. First-mover advantages. *Strategic Management Journal*, 9 (S1), 41-58.
- Loury, G. C., 1979. Market structure and innovation. *The Quarterly Journal of Economics*, 93 (3), 395-410.
- Malerba, F., Orsenigo, L., 2002. Innovation and market structure in the dynamics of the pharmaceutical industry and biotechnology: towards a history-friendly model. *Industrial and Corporate Change*, 11 (4), 667-703.
- Mansfield, E., 1986. Patents and innovation: an empirical study. *Management Science*, 32 (2), 173-181.
- Meng, R., 2008. A patent race in a real options setting: Investment strategy, valuation, CAPM beta, and return volatility. *Journal of Economic Dynamics and Control*, 32 (10), 3192-3217.
- Michel, J., Bettels, B., 2001. Patent citation analysis. A closer look at the basic input data from patent search reports. *Scientometrics*, 51 (1), 185-202.
- O'Donoghue, T., 1998. A patentability requirement for sequential innovation. *The RAND Journal of Economics*, 654-679.
- Raasch, A., 2006. *Der Patentauslauf von Pharmazeutika als Herausforderung beim Management des Produktlebenszyklus: Strategische Optionen und ihre erfolgreiche Umsetzung in Marketing und Vertrieb*, DUV, Wiesbaden.
- Rao, R. C., Rutenberg, D. P., 1979. Preempting an alert rival: Strategic timing of the first plant by analysis of sophisticated rivalry. *Bell Journal of Economics*, 10 (2), 412-428.
- Reinganum, J. F., 1983. Uncertain innovation and the persistence of monopoly. *American Economic Review*, 73 (4), 741-748.

- Reinganum, J. F., 1985. Innovation and industry evolution. *Quarterly Journal of Economics*, 100 (1), 81-99.
- Reinganum, J. F., 1989. The timing of innovation: Research, development, and diffusion. in: *Handbook of Industrial Organization*, North Holland, 849-908.
- Sandner, P., Ziegelbauer, K., 2008. Product-related research: how research can contribute to successful life-cycle management. *Drug Discovery Today*, 13 (9-10), 457-463.
- Scherer, F. M., 1975. *The economics of multi-plant operation: an international comparisons study*, Harvard University Press, Cambridge, MA.
- Schneider, C., 2008. Fences and competition in patent races. *International Journal of Industrial Organization*, 26 (6), 1348-1364.
- Schroth, E., Szalay, D., 2010. Cash breeds success: The role of financing constraints in patent races*. *Review of Finance*, 14 (1), 73-118.
- Schumpeter, J. A., 1934. *The theory of economic development*, Harvard University Press, Cambridge, Mass.
- Schumpeter, J. A., 1942. *Capitalism, Socialism and Democracy*, Harper, New York.
- Smiley, R. H., Ravid, S. A., 1983. The importance of being first: learning price and strategy. *Quarterly Journal of Economics*, 98 (2), 353-362.
- Smiley, R., 1988. Empirical evidence on strategic entry deterrence. *International Journal of Industrial Organization*, 6 (2), 167-180.
- Sternitzke, C., 2009. Defining triadic patent families as a measure of technological strength. *Scientometrics*, 81 (1), 91-109.
- Sternitzke, C., 2013. An exploratory analysis of patent fencing in pharmaceuticals: The case of PDE5 inhibitors. *Research Policy*, 42 (2), 542-551.
- Trott, P., 2008. *Innovation management and new product development*, 4th, Pearson, Harlow.
- Zizzo, D. J., 2002. Racing with uncertainty: a patent race experiment. *International Journal of Industrial Organization*, 20 (6), 877-902.

Table 1: Indications per US patent document

patent families with indications		58
US patent documents with indications	# different indications	179
	mean #indications per document	5.95
	std. dev. #indications per document	10.11
	min #indications per document	1
	max #indications per document	54

Table 2: Indications occurring in different patent documents

# of different families where an indication is mentioned in	
mean	2.51
std. dev.	2.75
min	1
max	18

Figure 1: Different indications mentioned by applicants.

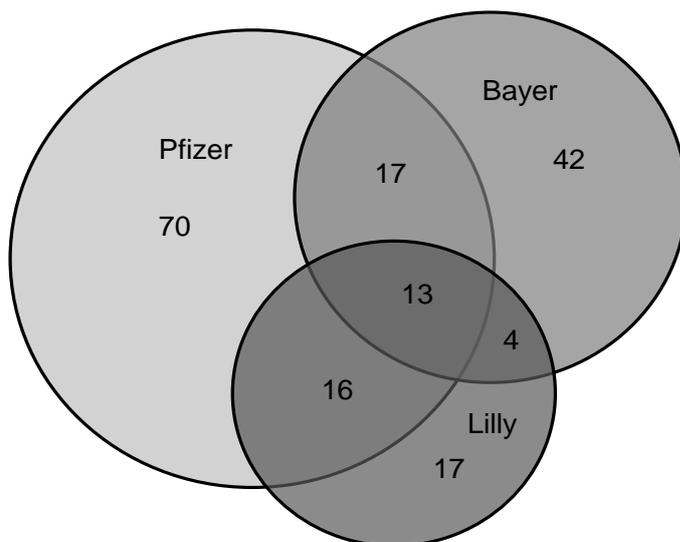


Figure 2: Sequential filings of the most highly claimed indications.

