Weak Patents Are a Weak Deterrent: Patent Portfolios, the Orange Book Listing Standard, and Generic Entry in Pharmaceuticals

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1. Introduction

A long legacy of empirical research suggests that patents are more important for stimulating research in pharmaceuticals than in any other industry (Levin et al. 1987; Cohen et al. 2000). Patents on new drug compounds are difficult to invent around, and thus are effective in preventing imitation. At the same time, without patents, imitation of existing therapies is comparatively easy. The very effectiveness of some drug patents has an obvious downside, which is to restrict access to low-price therapies in the meantime. Pharmaceuticals have been traditionally classified as a "discrete product" industry, in which relatively few patents cover a single product (Levin et al. 1987; Cohen et al. 2000). The ideal type arises when a single patent, covering a novel active ingredient, protects innovation on a newly available drug.

As we explain in this paper, this characterization is an increasingly poor fit. Brand-name firms have sought increasing recourse to ancillary patents to protect their market positions, including patents on chemical variants, alternative formulations, methods of use, and other relatively minor aspects of the drug. The result is a web of overlapping claims, which a generic drug maker must address or avoid in order to market a competing product. These patents are also conventionally viewed as "weak" patents (or

low quality patents) in the sense that if litigated to judgment, they are less likely to be found valid and infringed.

The resulting proliferation of drug patents is not confined to the United States. To take just one example, a sector report prepared by the European Commission reports a dramatic rise in the number of patents per drug, with some individual drugs having dozens of patents (European Commission 2009). The EU report and other commentators have referred to this phenomenon, and the resulting burden it places on generic competitors, as a patent "thicket." This term is problematic, however, because for some readers it evokes a fragmentation of intellectual property rights across multiple actors, and the challenges of with negotiating access to them (Shapiro 2003).

We use the alternative term "evergreening" to refer to patent proliferation that has the potential effect of prolonging brand exclusivity and delaying generic entry. We use the term advisedly, as we recognize the term has a negative connotation for some. It bears emphasis that in this paper, we make no claims about the welfare implications of these activities, though we speculate on these in the conclusion. One virtue of the term is that it highlights a distinctive temporal effect to the practice, compared to (some accounts of) thickets. In its simplest form, patents in a thicket tend to coincide temporally, so that multiple patents block entry at a point in time. By contrast, evergreening involves the accumulation of later expiring patents, with a view to extending the duration of the patent monopoly term.[1]

Evergreening is mediated by FDA regulatory practice. Here, we focus on a particular aspect of that practice, the FDA's establishment of criteria for which patents

[1] We use the term narrowly, to the exclusion of other life-cycle management practices, such as reformulations and product line extensions, to which the term is sometimes also applied.

may be "listed" as pertinent to a particular brand-name drug. Only certain types of patents may be listed. Listed patents are associated with each brand-name drug in an official FDA compendium called the "Orange Book."[2]

Listing has important consequences. In one respect, it makes the generic firm's life easier, by identifying which patents are most pertinent, thereby reducing uncertainty about the patent landscape for a particular drug. Ideally, the generic drug maker can simply refer to the Orange Book, rather than scour all patent listings for possibly pertinent patents. On the other hand, listing makes life harder for the generic firm. Among other effects, a generic firm must "challenge" every listed patent as invalid or not infringed, or else wait until patent expiration before the FDA approves its application. Thus, the listing process reduces some of the costs normally associated with thickets, while increasing others.

In recent and ongoing work (Hemphill 2011a, 2011b), some of which we report here, we have explored the buildup of listed patents, and concomitant increase of generic-firm efforts to offer a competing generic product prior to the expiration of those patents. A key result is the differential effect of different patent types, as reflected in the aspect of the drug that they cover. A patent covering the drug's active ingredient is less likely to be challenged. A patent covering an ancillary aspect of the drug, rather than the active ingredient, is more likely to be challenged.

In this paper, we examine the effects of different types of patents on generic entry.

[2] The official name is *Approved Drug Products with Therapeutic Equivalence Evaluations*. The publication lists those drugs that have been approved as safe and effective, and information about the availability of alternative "therapeutically equivalent" drugs, usually generic drugs. The "Orange Book" nickname refers to the initial choice of orange for the cover of the book's first edition, published in October 1980. Patent (and exclusivity) information was added to the Orange Book starting in 1985, after the passage of the Hatch-Waxman Act.

We extend our previous work by considering, as an additional type of "weak" patent, brand-name patents that are not listed in the Orange Book. Such unlisted patents might give rise to thicket-like concerns, particularly uncertainty about which patents are relevant to a particular technology. They are also a particularly salient form of weakness, to the extent that they have failed the Orange Book's test of pertinence. We develop a new measure of unlisted patents and examine their role in the growth of patent portfolios and effect on generic-firm attempts to offer a competing product, despite that portfolio. Surprisingly, we find little evidence that patent portfolio characteristics, including the number and characteristics of listed and unlisted patents, have an effect on the extent of genericization, or the timing of generic entry. In an effort to understand these results, we examine patent-by-patent litigation results for a sample of litigated patents.

We proceed as follows. In the next section, we explain the patenting and regulatory regime that governs drug competition, including patent listing standards, and review the debate about evergreening. In Section 3, we trace the growth of evergreening over the past 25 years, as measured by listed patents per drug, nominal duration of protection, acquisition of low-quality (non-active ingredient) patents, and unlisted (non-Orange Book) patents. Section 4 examines the effects of patents on generic entry and market life conditional on generic entry. We find only limited evidence that these patents matter for the extent of generic entry, or for effective market life conditional on generic entry. In Section 5, we explain this surprising result: the particular institutions created by the Hatch-Waxman Act, including patent listing standards and a special bounty to encourage generic firms to challenge brand-name patents, limit the strength of weak patents—whether non-active ingredient or unlisted (or both)—in this industry.

2. Regulatory Background: The Hatch-Waxman Act and Orange Book Patent Listing

New drugs have secured dramatic reductions in morbidity and mortality from disease during the last century (Murphy and Topel 2000). While the costs of drug discovery and safety and efficacy evaluation is high—some argue as high as $800 million (DiMasi et al. 2003)—the marginal cost of copying a drug is generally low. Once generic entry occurs, there is a dramatic reduction in price and increase in access. Given the importance of new drugs for health on the one hand, and the importance of generic entry for reduced prices and increased access on the other, appropriate calibration of the market exclusivity term of pharmaceuticals has long been a central concern to U.S. health and innovation policy.

The Drug Price Competition and Patent Term Restoration Act of 1984, commonly known as the Hatch-Waxman Act, established the modern regime for competition between brand-name and generic drugs. The Act provides a pathway for a generic firm to market a competing, "therapeutically equivalent" version of a brand-name drug by filing an Abbreviated New Drug Application, or ANDA, with the FDA. The most important requirement is bioequivalence, that the rate and extent of absorption of the active ingredient are the same between its proposed generic product and the brand-name drug. New clinical trials are not required.[3] This aspect of the Act is credited with a sharp increase in generic drug use, from less than 20 percent of prescriptions in 1984 (Frank 2007) to 78 percent in 2010 (IMS Institute for Healthcare Informatics 2011).

[3] The Act also conferred some benefit on brand-name firms. The "term restoration" part of the Act granted to the brand-name firm a term extension, one patent per drug, to make up for part of the time spent in lengthy pre-approval safety and efficacy studies.

Most new drugs are patent protected. If the generic firm chooses not to challenge any patents, then the FDA delays ANDA approval until expiration of the last listed patent. In many cases, however, the generic firm attempts to enter prior to patent expiration. In that case, the generic firm files an ANDA containing a "Paragraph IV" certification, asserting that one or more listed patents are invalid or not infringed by the proposed generic product. The filing of such an ANDA is an act of patent infringement, which often prompts a patent infringement suit by the brand-name firm. As discussed in part 5, however, the suit may not involve all of the challenged patents. This pattern—launch, challenge, sue—is frequent for major drugs. Nearly all of the top ten best-selling drugs of 2000, and again in 2005, had Paragraph IV challenges (Hemphill 2006, 2009).

The Orange Book listing process both facilitates and necessitates these patent disputes. As noted in the Introduction, the Act requires brand firms to list most pertinent patents. For patents issued before NDA approval, a brand-name drug maker is required to list any patent containing at least one claim that covers the drug's active ingredient, its formulation, or any method of use pertaining to an approved indication. For patents issued after NDA approval, listing is not required, but there is a strong incentive to list.

The incentive comes from the generic firm's obligation, when it files its ANDA, to challenge every listed patent or else wait until patent expiration before receiving FDA approval.[4] All brand-name patents listed before ANDA filing are subject to this obligation. Moreover, listing provides an additional advantage in litigation. When the brand-name firm files a suit on a timely listed patent, the generic firm is subject to an automatic stay of FDA approval for up to 30 months, while the patent suit is considered

[4] There is an exception. If patent covers a method of use for which the generic firm does not seek FDA approval, the generic firm can make a "section 8" filing as to that patent, rather than a Paragraph IV certification.

by the district court.[5]

The brand-name firm's decision to list has an ancillary benefit for the generic firm. Under certain circumstances, the first generic firm to file an ANDA is entitled, upon FDA approval, to a 180-day exclusive right to market its product in competition with the brand-name firm before other generic firms may enter. This special bounty provides an incentive for a generic firm to challenge a brand-name patent, helping to overcome collective action problems among generic firms in challenging patents. Listing can provide a benefit to the generic firm where there is a strong, hard-to-challenge patent expiring at t_1, and a weaker patent expiring at t_2. The second patent provides a realistic basis for the exclusivity, which would not have been conferred by the first patent alone.

Not all patents are listed in the Orange Book. Methods of manufacturing the drug, for example, are prohibited. So are formulations that do not cover the marketed drug product, and methods of use covering unapproved indications. For patents issued after NDA approval, listing is not required, and despite the incentives discussed above, not all eligible patents are actually listed. Brand-name drug makers are free to assert unlisted patents against generic drug makers.

Unlisted patents are part of a generic firm's patent clearance search, the determination of which patents stand in the way of attempted entry (Rumore 2007). Such patents may be harder for generic firms to identify and plan around. Unlisted patents are the source of patent litigation between brand-name and generic firms,[6] but much less

[5] In practice, the "30 month stay" is generally shorter than that, because measured from the brand-name firm's receipt of notice of the ANDA with a Paragraph IV certification, not the start of patent litigation.

[6] For example, a recent Paragraph IV litigation surrounding the antihistamine Allegra the brand firm also asserted patents covering fexofenadine intermediates and methods of making the product (Rumore 2007).

frequently than listed patents.

3. Pharmaceutical Patenting Since Hatch-Waxman

We begin our analysis by reporting changes over time in patenting, over the 25 years since the Hatch-Waxman Act was passed. We restrict attention to drugs that contain a novel active ingredient, so-called new molecular entities, or NMEs. NMEs are generally considered to be among the most innovative drugs. Our data is the set of 382 NMEs approved by the FDA between 1985 and 2002.

As detailed in Hemphill and Sampat (2011a), for each drug, we collected information about applicable patent protection from current and archival editions of the Orange Book (FDA 1985-2009). Our first measure is the number of unique patents listed in any edition of the Orange Book. A second measure is the lag between a drug's approval date and the date of the last-expiring patent, which we call the "nominal" patent term.

Figure 1 shows an increase in the mean and median number of listed patents per drug over this period.[7] The mean value increased from about 2 to nearly 4 patents per drug, and the median increased from 1 to 3 patents per drug. Since the data are right-censored, these trends may understate the extent of growth of patenting. Figure 2 shows that nominal patent term has also increased over this period, from about 14 to over 16 years by the late 1990s, and only slightly lower in the most recent cohort.

To better understand the nature and extent of evergreening, we also coded the

[7] These figures differ slightly from those reported in Hemphill and Sampat (2011a) in two respects. First, here we examine NMEs rather than new chemical entities (NCEs). The main difference is that a drug that contains a novel active ingredient, but also a previously approved active ingredient, is an NME but not an NCE. Second, we include injectable drugs, excluded from the previous analysis.

strength of each listed patent, based on whether the patent claims the active ingredient. Active ingredient patents ("AI patents") are relatively likely to be valid and infringed by a bioequivalent generic product, compared to non-AI patents. It is harder to establish their invalidity, as this would require showing the drug was previously disclosed or that the patentee engaged in inequitable conduct during the application process. Non-infringement is even more difficult, at least for the NMEs that we consider here, since by definition, bioequivalent drugs will infringe.

We worked with a former PTO examiner of drug patent applications to code each patent according to whether it contained at least one active ingredient claim. In other words, a patent with both active ingredient and non-active ingredient claims counts as an AI patent. As discussed elsewhere (Hemphill and Sampat 2011a, b) the goal is to capture "basic" compound patents, as opposed to patents on ancillary aspects of the drug. For example, patents covering the particular formulation or composition of the drug, or methods of use, are coded as non-AI patents. We take a narrow view of AI status. Thus, patents on alternative isomers, crystalline structures, salts, and metabolites are also coded as non-AI patents.

We examined the construct validity of these measures in two ways. First, we determined which patent on an NME is selected for "patent extension." Under the restoration provisions of Hatch-Waxman, one patent per drug can be extended to compensate the drug maker for delays during the FDA review process, and a branded drug maker thus has a strong incentive to extend a patent that is likely to be found valid and infringed by potential generic products. A much higher share of AI patents was extended than non-AI patents (79 percent versus 13 percent). Second, we examined the

timing of AI versus non-AI patents, under the view that more basic patents would be applied for earliest. We find that of the patents we have characterized as AI patents, 77 percent are the first filed patents (by application year) for the drug, compared to just 17 percent of non-AI patents.

Figure 3 shows that the share of NMEs with a listed non-AI patent increased sharply over this period, from less than 60 percent to about 85 percent, with particularly sharp increases over the 1990s. Taken together, the data provide strong evidence of growing aggressiveness in patenting by pharmaceutical firms over this period, consistent with allegations about growth of evergreening.[8]

What about unlisted patents? By definition, these are difficult to identify, since there is no official accounting of them. We developed a rough measure of unlisted patents by identifying all patents that shared priority with a listed drug—that is, all U.S. issued patents in the same patent family. This information was obtained from the USPTO "related application" data. Specifically, for each listed patent we determined all parent and child applications that resulted in issued patents.[9]

The NMEs approved over this period had 1122 listed patents. The listed patents shared priority with 717 unlisted patents. We did not individually code the unlisted

[8] The growth of ancillary patents may also have implications for use of patent-based statistics as economic indicators. Graham and Higgins (2007) find that firm level correlations between new product introductions and drug patenting (based on Orange Book patents and a firms overall patenting in pharmaceutical patent classes) during 1985-2001 are quite low, in contrast to work by Comanor and Scherer (1969) showing a strong relationship between the two in the 1950s. The authors suggest this raises questions about the uses of patents as proxies for innovation in this industry. Our findings at the product level, showing that patents per drug are increasing over time, are consistent with this. While these ancillary patents are weaker in the legal sense, i.e., less likely to prevent the entry of a therapeutically equivalent generic product, we are agnostic as to whether the patents represent less innovation. This is related to issues surrounding the "innovativeness" of incremental innovations in pharmaceuticals (Berndt et al. 2006, Wertheimer and Santella 2005), and those surrounding whether patent standards of innovativeness (novelty and non-obviousness) are aligned with the health benefits from new drugs (Roin 2009).

[9] Since U.S. patent applications that did not result in grants were not published until 1999, we cannot examine pending patent applications. This is a significant omission, since these applications could also create uncertainty for potential generic applicants.

patents as AI or non-AI patents. Treating the listed and unlisted patents as components of the "full" patent portfolio, unlisted patents account for 40 percent of the total. Moreover, as Figure 4 demonstrates, this accumulation of unlisted patents has also been increasing over time. Taken together, these results suggest that brand-name drug makers are patenting more aggressively, seeking more low-quality listed patents, extending the nominal patent term, and accumulating more unlisted patents.

4. Patent Portfolio Characteristics and Generic Entry

4.1 Extent of Genericization

At first glance, the growth of patenting depicted in Part 3 would seem to confirm some commentators' worst fears about evergreening. However, as explained in Part 2, there is a unique opportunity to challenge and perhaps avoid the effect of these patents, which could limit their effect. In this section, we explore how patents and other drug characteristics affect the likelihood of entry and effective market life conditional on entry.

Data

Here, we examine a second dataset, NMEs approved between 1992 and 1996 that have at least one listed patent. For each drug, we collected the same information about the drug's patent portfolio described above. We also constructed, as additional patent measures, the number of AI patents and non-AI patents for each drug. For each drug, we collected the route of administration, on the view that orally administered drugs are easier to reverse engineer and imitate, and therapeutic class (Department of Veterans Affairs

2011).

To measure market potential, we calculated brand-name sales in year 5 after approval, using the National Sales Perspective database of IMS Health, the leading commercial provider. Sales at this point reflect market potential of the drugs, but are unlikely to reflect actual generic entry.[10] We inflated sales to 2010 values using the CPI deflator (BLS 2010). Since our focus is on marketed drugs, we dropped three drugs with no reported sales, leaving a final sample of 116 drugs.

We observe generic entry as of the end of 2011. We define generic entry as approval of a therapeutically equivalent (TE) ANDA.[11] For the generic product, we restrict attention to drugs that are bioequivalent to the brand-name drug and received an "A" rating of therapeutic equivalence from the FDA. We limit attention to TE generic drugs because non-TE generics aren't close competitors. They fail to trigger automatic substitution under state law and formulary rules, and thus generally achieve much lower market penetration. We collected this information from an FDA listing of therapeutic equivalents called Drugs@FDA. Since Drugs@FDA does not provide information on therapeutic equivalence for brand drugs that have been discontinued, we supplemented this information with data from archival versions of the Orange Book products file, which allow us to determine whether the drug was ever the subject of therapeutically equivalent generic entry.

While we can reliably determine from these sources whether a drug has generic

[10] Of the NMEs that comprise our sample, nearly all are NCEs. For NCEs, no ANDA containing a Paragraph IV certification may be filed during the first four years after drug approval. (The relevant data exclusivity is sometimes referred to as "five-year exclusivity," but the period is shorter in the case of a Paragraph IV certification. 21 U.S.C. §355(j)(5)(F)(ii).)

[11] That is, we only count drugs that are deemed bioequivalent to the brand-name drug and received an "A" rating of therapeutic equivalence from the FDA.

equivalents, it is more difficult to assess exactly when first generic entry occurred. However, beginning in 2001 the FDA began publishing a "first time generics" list that provides this information. Accordingly, we also constructed an indicator of whether a drug experienced first generic entry within 15 years.

Table 1 shows the distribution of these variables. About three-fifths of the drugs approved between 1992 and 1996 had experienced generic entry by the end of 2011, and about 40 percent experienced generic entry within 15 years. The sample includes drugs that range from those with trivial sales to blockbusters. The top selling drug is Lipitor, with $5 billion in sales in its fifth year after approval. About half of the drugs are orally administered. Interestingly, while the mean number of listed patents exceeds the mean number of unlisted patents, the number of unlisted patents is more variable. On average, the drugs have about one AI patent and 2 non-AI patents.[12] Consistent with the aggregate descriptive statistics depicted in Figure 2, average nominal patent term exceeds 16 years.

Analyses

We begin by estimating linear probability models relating whether there was a generic entry on a drug (by 2011) to drug characteristics, sales in year five, and other patent portfolio characteristics. Each of the models includes indicators for drug class and brand approval year.

Table 2 shows results. In the baseline model, reported in Column 1, sales have a positive and significant effect on the likelihood that a drug experienced generic entry by 2011. As expected, oral dosage forms are also more likely to draw generic entry, but the

[12] Multiple AI patents can occur for several reasons, including when an early patent claims a genus of compounds, and a later patent covers the specific active ingredient of the drug.

effect is statistically insignificant. Column 2 shows a first surprising result: the total number of listed patents on a drug has no qualitatively or statistically significant effect on genericization. In Column 3, we break out counts of AI and non-AI patents, finding that neither has an effect. Nor does nominal patent term from listed patents (Column 4). In Column 5 we introduce counts of unlisted patents on a drug, finding a positive and insignificant association with genericization, suggesting that these patents also do not appear to deter generic entry.

In the models in Columns 1 through 5 we examined all patents on a drug. However, it is possible that generic entry also affects accumulation of patents, i.e., causality is in the opposite direction. To account for this possibility, in the models reported in Columns 6 and 7 we restrict the set of patents to those issued within 5 years of brand approval. Generic entry ordinarily cannot occur before this time due to data exclusivity rules. In these models too the number and quality of patents do not have a significant association with whether a drug went generic as of 2011. Column 8 breaks out counts of early listed and unlisted patents, and shows that neither has an effect.[13]

Table 3 shows results from models where the dependent variable is whether generic entry occurred within 15 years, giving each approval year cohort an identical window for potential generic entry. The results are similar to those from the baseline analyses.

Overall, the results suggest that while market size matters for genericization, the number or quality of patents on a drug do not. This is surprising. However, it is possible that patent portfolios affect the *timing* of generic entry—by delaying the decision to file

[13] We obtain similar non-results from logit models, and from models with different transformations of the patent variables (dichotomous measures rather than counts, and natural logs of patent counts).

an ANDA—even if they do not matter for *whether* entry eventually occurs. Since we lack information on precise timing of first generic entry for this sample, we cannot examine this directly. In the next section we address this directly, using a dataset in which we are able to measure the duration of brand exclusivity.

4.2. Do More Patents Influence Effective Market Life?

Data

This analysis builds on our prior examination of Paragraph IV patent challenges and effective market life (Hemphill and Sampat 2011b). Here, our dataset is the 123 NMEs that were first subjected to competition from a TE generic product between 2001 and 2010.[14] We examine the same variables as before,[15] but now using a set of drugs in which generic entry has occurred.

Our primary measure of effective market life is the time from brand approval until final FDA approval of the TE generic product. This measure of market life differs slightly from that used in previous analyses (e.g. Grabowski and Kyle 2007), which use a measure of generic launch rather than approval. We also examine this alternative measure in a robustness check. The difference between the two may be particularly relevant for considering the effects on unlisted patents: even if a generic firm secures ANDA approval from the FDA, it might delay a launch, in part due to the overhang of unlisted patents.

Table 4 shows descriptive statistics on these variables.

[14] In Hemphill and Sampat (2011b) we focused only on drugs with drugs eligible for patent challenges, so the sample size there was 119 rather than 123.

[15] The patent measure is slightly different, limited to those patents issued prior to generic entry, on the view that patents issued after entry are not expected to affect generic entry.

Results

Table 5 relates our primary measure of effective market life to drug characteristics. The drug sales measure does not matter for effective market life. However, consistent with the impression that these drugs are easier to reverse engineer, effective market life is significantly lower for orally administered drugs. The number of listed patents is not significantly associated with effective market life (Column 2). Column 3 shows that while the count of strong (AI) patents is associated with longer market life, this effect, like the effect of the number of weaker (non-AI) patents, is insignificant. Even nominal patent term is unrelated to actual effective market life (Column 4). Overall, the number, nature, and duration of listed patents have no straightforward relationship with effective market life. However, Column 5 does show that that the number of unlisted patents on a drug has a statistically significant positive association with effective market life. All else equal, a one standard deviation increase in the number of unlisted patents is associated with about an 8-month increase in effective market life.

What if we instead employ the alternate measure of market life, time to generic launch? Table 6 reports point estimates that are qualitatively similar to Table 5. Nominal patent term is now positive and significant at the 10 percent level (it was insignificant in the previous analysis), and the count of unlisted patents is positive and significant at the 10 percent level (previously significant at the 5 percent level).

Though there has been much concern about evergreening in this industry, we find that weak patents, though much more prevalent in recent years, do not appear to have a

strong effect on the final outcome of generic entry. Nor do unlisted patents, which might be expected to discourage generic entry, consistently matter. The effects of nominal patent term on generic entry are also weak.

5. The Explanation: Paragraph IV Challenges

5.1 Previous Research

What explains this weakness of weak patents in pharmaceuticals? We believe the explanation is the patent listing and challenge regime unique to this industry. As noted, Paragraph IV challenges provide a means for a generic firm to pursue entry when it believes the relevant patents to be invalid or not infringed.

Paragraph IV challenges are an important source of generic competition (FTC 2002; Grabowski 2004; Hemphill 2006). Hemphill and Sampat (2011a) show that these have risen sharply over time: about 20 percent of drugs approved between 1985 and 1987 drew challenges, compared to over 50 percent of drugs approved between 2000 and 2002. For this very reason, they are a controversial feature of the Hatch-Waxman regime (Engelberg 1999; Higgins and Graham 2009).

Grabowski (2004) and others take the view that these challenges are indiscriminate, targeting high sales drugs rather than low quality patents. For example, Voet (2006) asserts that "the validity of virtually all major patented drugs is being challenged not necessarily because they are not meritorious patents, but only because that is the road to riches." The argument is that they are pursuing a "prospecting" strategy—challenging many brand-name products in the hope of winning a few of them, and thus increasing uncertainty and reducing innovation incentives for brand-name firms

(Grabowski 2004; Higgins and Graham 2009). Gal and Shari (2007) report a widespread sense that generic firms are "legal sharks that take advantage of loopholes" in the Hatch-Waxman Act. Higgins and Graham (2009) suggest that Paragraph IV challenges reduce effective patent life, thereby "diminish[ing] industry revenues and profits," and "contribut[ing] to the current crisis in industry R&D pipelines."

In two previous papers we have argued against this conventional view of patent challenges. Hemphill and Sampat (2011a) examines all drugs approved between 2000 and 2008, to assess factors affecting the hazard that the drugs attract Paragraph IV challenges. There we find evidence that market size (proxied, as in the other analyses discussed above, by brand-name drug sales) does have a strong effect on the likelihood of a patent challenge. But patent strength also matters: drugs with non-AI patents, particularly those that extend nominal patent term, are significantly more likely to draw challenges. Thus weak patents—defined, as noted above, as those that if litigated to judgment, will be found valid and infringed—particularly term-extending weak patents, are most likely to draw challenges.[16] This view suggests the characterization of challenges as frivolous attacks that reduce market life is too simple. Rather, patent challenges may also be important for preventing welfare losses to consumers from low-quality patents.[17]

One concern in interpreting those results causally is the potential that challenges and patent accumulation are responsive to some third factor (e.g. market potential not

[16] We also found that off the shelf measures of patent quality, including citations and family size, are also related to challenges: drugs with lower quality patents, by these measures, were more likely to attract challenges. However, these measures are more related to the private value of patents than the strength of patents as we define it above.

[17] Branstetter et al. (2011) estimate the static welfare gains from Paragraph IV challenges for hypertensive drugs alone to be over $90 billion over the 1997-2008 period.

captured by measured sales) or that anticipation of challenges (to the strong patents) is compelling firms to accumulate more ancillary patents for defensive reasons.

In Hemphill and Sampat (2011b) we developed a second empirical strategy to address this concern. There, we examined all 119 NMEs with successful generic entry between 2001 and 2010 and at least one patent eligible for challenge (a subset of the sample employed in Section 4.2 above).

These drugs included 319 patents, of which 190 were challenged. We showed that of the patents challenged, more than 80 percent were non-AI patents. And the likelihood of challenge to AI patents was much lower than the likelihood of challenge to non-AI patents: 29 versus 75 percent. We also estimated models with drug fixed effects to show that even within drugs, the likelihood of challenge was significantly higher for non-AI patents, and those that extended nominal patent term. This provides further evidence that challenges are not just about prospecting, but rather are disproportionately targeting lower quality patents and late expiring patents. These results help explain why, contrary to previous predictions (Grabowski and Kyle 2007), effective market life has remained stable over the past decade despite a rise in the frequency and alacrity of challenges. We also show that even though challenges are more common for higher sales drugs, there is no difference in effective market life across the sales distribution: challenges are responding to evergreening, which is more common for higher sales drugs, and help ratchet effective market life back to about 12 years, what it has been over the much of the post-Hatch-Waxman era.

5.2 New Evidence from Patent Litigation Outcomes

Hemphill and Sampat (2011b) did however provide limited evidence consistent with prospecting: in some models, challenges to AI patents are increasing with drug sales. We speculated that generic challenges to AI patents were unlikely to be successful, and provided indirect evidence on this by showing such challenges are not significantly related to effective market life. Here, we examine the outcomes of challenges to AI and non-AI patents directly. For the 190 patents that were challenged (associated with 78 drugs) we examined which were actually litigated, using information from Paragraph Four Reports (a commercial vendor), the Stanford IPLC database (now called Lex Machina), ANDA approval letters, SEC filings, and press releases.

Table 7 shows that of the 190 patents that were challenged, only 107 were litigated. The majority of the litigated patents are non-AI patents (80 percent), not surprising since non-AI patents are the great majority of challenged patents. But the likelihood of a brand litigating a challenged patent is significantly greater for AI patents than non-AI patents (68 percent versus 54 percent), suggesting brand's belief in the strength of these cases.

For each patent that was litigated, we also determined outcomes of this litigation as of the end of 2011. We focus here on patents where there is a clear win for generics or brands, excluding 36 patents that result in settlements and 4 patents that expired during litigation. Settlements, particularly those involving payments for delayed entry, are an important policy issue in assessment of Hatch-Waxman patent challenges: in ongoing work we are examining the types of patents that settle, and whether settlements are more like brand or generic wins in their effects on timing of entry. Patents that expire during

litigation are also difficult to classify as brand or generic wins.

Table 8 relates litigation outcomes to patent type for the 67 patents where there is a clear brand or generic win. Generics win 83 percent of litigation over non-AI patents, and brands win 85 percent of litigation over AI patents. These results suggest that once subjected to litigation, neither prospecting nor evergreening appear to be all that successful.

5.3 What About Unlisted Patents?

While we do not have information about litigation of unlisted patents for these drugs, evidence from other sources suggests that assertion of these patents is rare. For a set of 363 drugs with Paragraph IV challenges (as to at least one patent) listed in Paragraph Four Reports, we compiled information on which patents were litigated. Overall, 638 distinct patents were litigated. Of these, only 49 (about 8 percent) were unlisted patents.[18] While it is difficult to demonstrate whether the rareness of litigation on these patents is due to their weakness or the absence of procedural advantages that accompany Orange Book listing, and we do not have information on outcomes of litigation on these patents, the fact that they are such a small share of patents asserted in litigation provides at least some evidence of the relative unimportance of unlisted patents for generic entry in pharmaceuticals.

The difficulties brands appear to face in successfully defending non-AI patents, and difficulties in successfully litigating unlisted non-Orange Book patents, likely help reconcile the results from the descriptive analyses in Section 3 with the regression

[18] Of the 589 Orange Book patents that were litigated the vast majority (493, or about 84 percent) are non-AI patents, consistent with the figures reported above on the types of patents involved in litigation.

analyses in Sections 4 and 5. Despite the growth of ancillary patenting—evidence of evergreening—non-AI patents listed on the Orange Book are routinely challenged and do not matter much for generic entry. Unlisted patents are also increasingly common, but rarely asserted in patent litigation.

6. Conclusion

In the quarter century since the passage of Hatch-Waxman, the practice of listing ancillary term-extending patents on the Orange Book has been growing rapidly. On average, these patents are weak in the sense of Farrell and Shapiro (2008): They are of less certain validity and/or less likely to be infringed, compared to active ingredient patents. Unlisted drug patents have also been growing. In light of these trends, current concern about evergreening is understandable.

In pharmaceuticals, as in other industries, weak patents result because it is difficult for resource-constrained patent offices to thoroughly evaluate the hundreds of thousands of applications they receive annually. Theoretical work suggests these weak patents can be unexpectedly strong in their ability to exclude rivals or provide a basis for extracting royalties (Farrell and Shapiro 2008).

In this sector, however, weak patents appear … relatively weak. There is only limited evidence that unlisted patents matter for competition, and they are rarely asserted in pharmaceutical patent litigation. And listed non-AI patents do not have a strong effect on the extent of generic entry, or the duration of market exclusivity period. The longer nominal patent term sustained by such patents is not associated with longer effective market life.

We have suggested the reason why. The Hatch-Waxman patent listing and challenge rules, underpinned by the bounty available to a first generic firm challenging brand-name patents, create a setting where potential competitors are able and willing to give a strong second review to weak patents listed on the Orange Book.

Without the listing, challenge, and bounty features of Hatch-Waxman, aggressive drug patenting would almost certainly delay generic entry in the United States. The U.S. setting may be unique, however. A lack of similar institutions in other jurisdictions may explain why our findings diverge from those of the EU Sector Report, which suggests strong effects of evergreening on competition in European pharmaceutical markets. Numerous developing countries, lacking robust institutions for *ex post* review of patents, have instead sought to limit non-active ingredient patents in pharmaceuticals *ex* ante through higher patentability standards and patent subject matter restrictions (Deere 2009).

Lemley (2001) has considered the costs and benefits of more thorough *ex ante* versus *ex post* review of patents, and suggested the latter is be more efficient given the difficulty in identifying important patents early on, and resource constraints facing patent offices. Hatch-Waxman bounties create strong incentives for generics to identify and force *ex post* review of questionable patents on important drugs, and might be seen as an example of the rational ignorance concept working.

However, there are significant transaction costs associated with this system. First, though we argue claims that patent challenges are only about prospecting are overstated, surely some prospecting is occurring. In other words, patent bounties could encourage not only challenges that are likely to succeed, but low probability shots in the dark. Second, the regime is costly. Our previous work (Hemphill and Sampat 2011b) suggests that the

interplay of patent listing and challenges has resulted in a stalemate: branded firms acquire patents to extend term (especially for big drugs), generics challenge them, and net effective market life is stable across drugs and over time. These activities, while creating legal activity and costs, effectively cancel one another out.

There may be better ways to achieve this. The pharmaceutical industry is a unique sector where more thorough review at an intermediate stage is possible, since Orange Book listings disclose commercially important patents soon after a product is approved. We previously suggested that a requirement that patents be subject to immediate re-examination upon listing would help limit the need for some challenges, and may be a less costly way to scrutinize these patents (Hemphill and Sampat 2011b).[19]

If evergreening is futile, why do brands acquire weaker term-extending patents? It is possible that there are effects we aren't seeing. Additional patents may affect the number of generic entrants and patent challenges, even if they don't influence whether there is at least one generic entrant or the timing of entry. It is also possible that while weak patents don't matter for entry on average, they do for a handful of drugs. In an industry that is heavily reliant on blockbusters, when a few months of extra exclusivity on these drugs can be extremely valuable, low-cost stockpiling of additional patents on drugs (even before market potential is known) may be economically rational. Finally, additional patents may change the bargaining power of brand firms in Hatch-Waxman litigation, and may help sustain better settlements, a topic we are currently exploring.

All of this assumes that weak patents are undesirable: that pharmaceutical companies should not enjoy market exclusivity from patents that would not meet

[19] However, this would not eliminate the need for non-infringement challenges, only invalidity challenges.

patentability requirements if rigorously examined. A broader question, beyond the scope of this paper, is whether patents that are of questionable validity are nonetheless important for innovation incentives, i.e., if patent standards are perhaps misaligned with innovativeness or the health impact of new drugs in this industry (Roin 2009).

References

Berndt, Ernest R., Iain M. Cockburn, and Karen A Grépin. 2006. The Impact of Incremental Innovation in Biopharmaceuticals. Drug Utilisation in Original and Supplemental Indications. *PharmacoEconomics* 24(2): 69-86

Branstetter, L., Chatterjee, C., Higgins, M. 2011. Regulation and Welfare: Evidence from Paragraph IV Generic Entry in the Pharmaceutical Industry. NBER working paper 17188.

Bureau of Labor Statistics. 2010. CPI Inflation Calculator. http://www.bls.gov/data/inflation_calculator.htm.

Cohen, Wesley M., Richard R. Nelson, and John P. Walsh. 2000. Protecting Their Intellectual Assets: Appropriability Conditions and Why U.S. Manufacturing Firms Patent (Or Not). National Bureau of Economic Research Working Paper No. 7552.

Comanor, William S., and Frederic M. Scherer. 1969. Patent Statistics as a Measure of Technical Change. *Journal of Political Economy* 77:392–398.

Deere, Carolyn. 2009. *The Implementation Game.* Oxford University Press.

DiMasi, Joseph A., Ronald W. Hansen, and Henry G. Grabowski. 2003. The Price of Innovation: New Estimates of Drug Development. *Journal of Health Economics* 22:151–185.

Engelberg, Alfred B. 1999. Special Patent Provisions for Pharmaceuticals: Have They Outlived Their Usefulness? *IDEA: The Journal of Law and Technology* 39:389–428.

European Commission. 2009. *Final Report, Pharmaceuticals Sector Inquiry*.

Federal Trade Commission. 2002. *Generic Drug Entry Prior to Patent Expiration.*

Food and Drug Administration. 1985–2009. *The Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations.*

Food and Drug Administration. 2009. *Drugs@FDA*. http://www.accessdata.fda.gov/Scripts/cder/ DrugsatFDA.

Frank, Richard G. 2007. The Ongoing Regulation of Generic Drugs. *New England Journal of Medicine* 357:1993–1996.

Gal, Ronny, and Shari Nikhil. 2007. Predicting Para IV: Generic Companies Have the Upper Hand in Formulation Patent Cases. *Bernstein Research Report*.

Grabowski, Henry G. 2004. Are the Economics of Pharmaceutical R&D Changing? Productivity, Patents and Political Pressures. *PharmcoEconomics* 22 (Supp. 2):15–24.

Grabowski, Henry G., and Margaret Kyle. 2007. Generic Competition and Market Exclusivity Periods in Pharmaceuticals. *Managerial and Decision Economics* 28:491–502.

Graham, Stuart J.H., and Higgins, Matthew J. 2007. Comanor and Scherer Revisited: Do Patents Proxy for New Product Innovations? Working Paper.

Hemphill, C. Scott. 2006. Paying for Delay: Pharmaceutical Patent Settlement as a Regulatory Design Problem. *New York University Law Review* 81:1553–1623.

Hemphill, C. Scott. 2009. An Aggregate Approach to Antitrust: Using New Data and Rulemaking to Preserve Drug Competition. *Columbia Law Review* 109:629–688.

Hemphill, C. Scott, and Bhaven N. Sampat. 2011a. When Do Generics Challenge Drug Patents? *Journal of Empirical Legal Studies* 8:613-649.

Hemphill, C. Scott and Bhaven N. Sampat. 2011b. Evergreening, Patent Challenges, and Effective Market Life in Pharmaceuticals. Working Paper, http://ssrn.com/abstract=1830404.

Higgins, Matthew J., and Stuart J.H. Graham. 2009. Balancing Innovation and Access: Patent Challenges Tip the Scales. *Science* 326:370–371.

IMS Institute for Healthcare Informatics, 2011. The Use of Medicines in the United States: Review of 2010.

Lemley, Mark A. 2001. Rational Ignorance at the Patent Office. *Northwestern University Law Review* 95:1495–1532.

Levin, Richard C., Alvin K. Klevorick, Richard R. Nelson, and Sidney G. Winter. 1987. Appropriating the Returns from Industrial Research and Development. Pp. 783–832 in *Brookings Papers on Economic Activity (Special Issue)*.

Murphy, Kevin, and Robert Topel. 2000. *Measuring the Gains from Medical Research: An Economic Approach*. Chicago, Ill: University of Chicago Press.

Roin, Benjamin N. 2009. Unpatentable Drugs and the Standard of Patentability. *Texas Law Review* 87:503-570.

Rumore, Martha M. 2007. Patent Law, Trademarks and Copyrights. In Delbert D. Konnor, *Pharmacy Law, Desk Reference* (125-143). Haworth Press.

Scott Morton, Fiona. 1999. Entry Decisions in the Generic Pharmaceutical Industry. *Rand Journal of Economics* 30:421–440.

Shapiro, Carl. 2003. Antitrust Limits to Patent Settlements. *Rand Journal of Economics* 34:391–411.

Thomas, John R. 2009. Patent "Evergreening": Issues in Innovation and Competition.

Thomas, John R. 2005. *Pharmaceutical Patent Law*. Washington, D.C.: BNA Books.

Voet, Martin A. 2005. *The Generic Challenge: Understanding Patents, FDA and Pharmaceutical Life-Cycle Management*. Boca Raton, Fla.: Brown Walker Press.

Wertheimer, Albert I., and Thomas. M. Santella. 2005. Pharmacoevolution: the advantages of incremental innovation. IPN Working Papers on Intellectual Property, Innovation and Health.

Figures and Tables

Figure 1: Patents per drug by approval cohort for new molecular entities (NMEs) approved 1985 to 2002

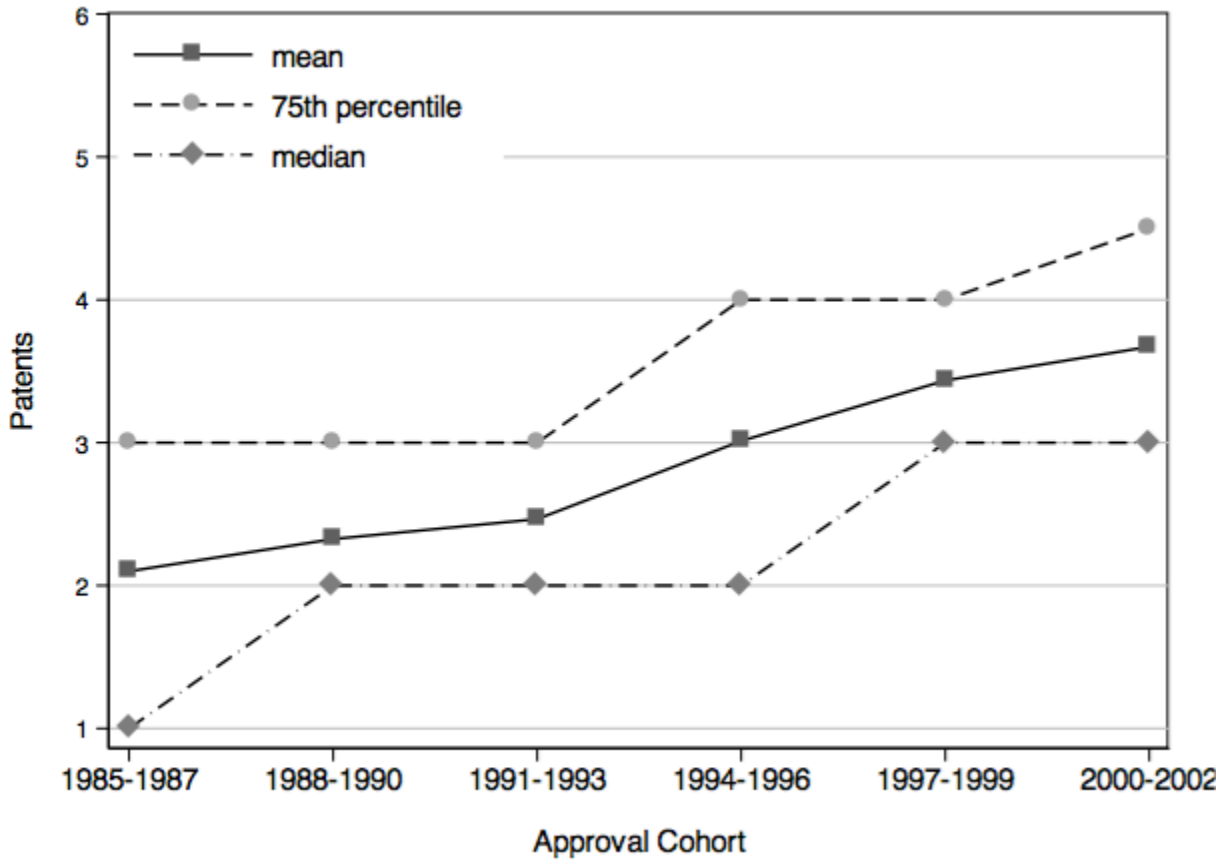

Figure 2: Nominal patent term by approval cohort for new molecular entities (NMEs) approved 1985 to 2002

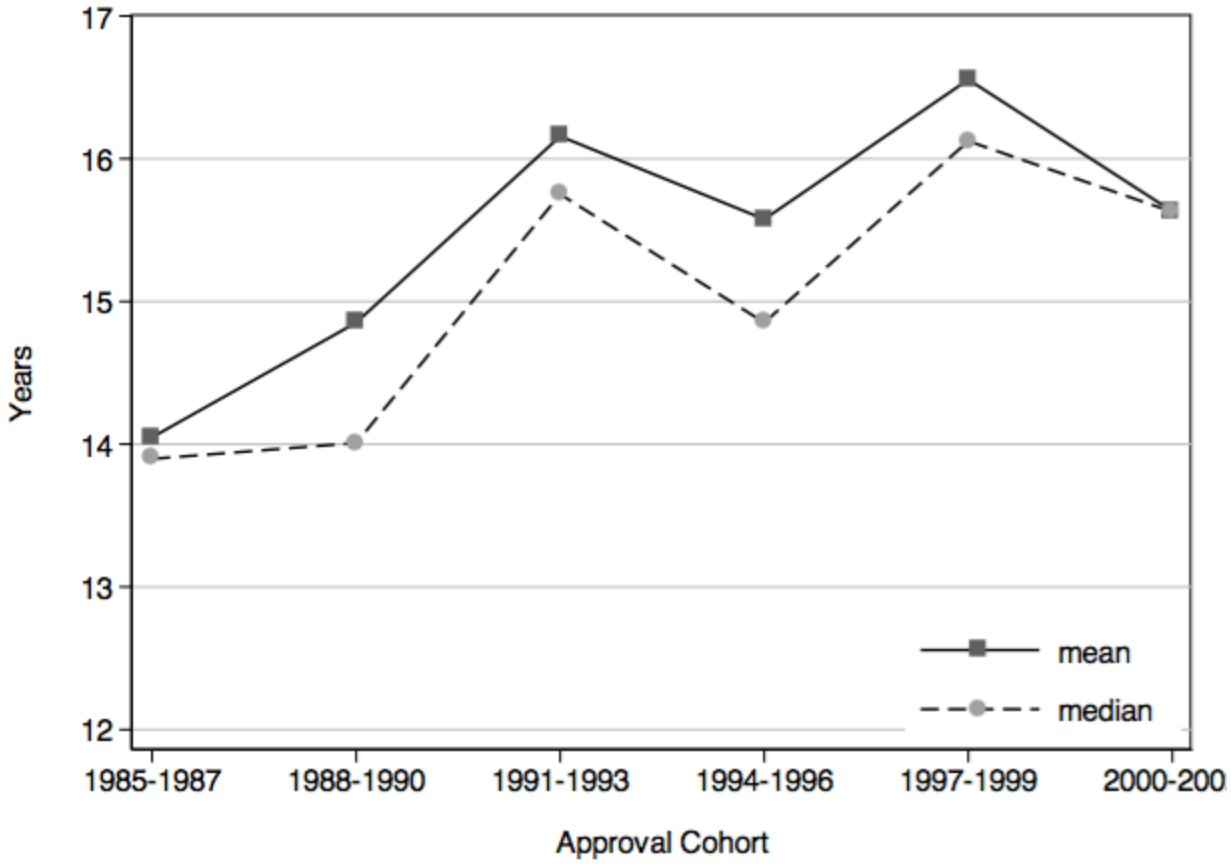

Figure 3: Share of drugs with non-AI patent by approval cohort for new molecular entities (NMEs) approved 1985 to 2002

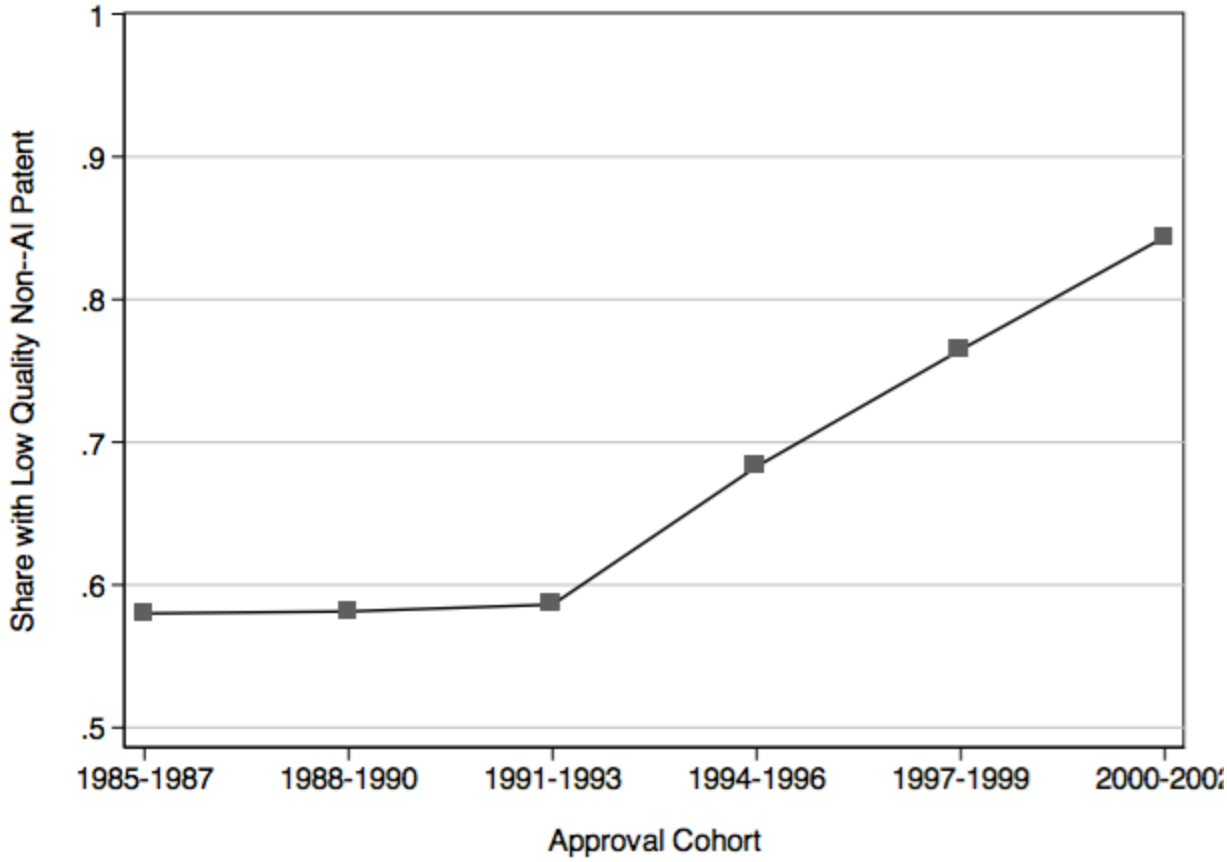

Figure 4: Non-Orange Book patents per drug by approval cohort for new molecular entities (NMEs) approved 1985 to 2002

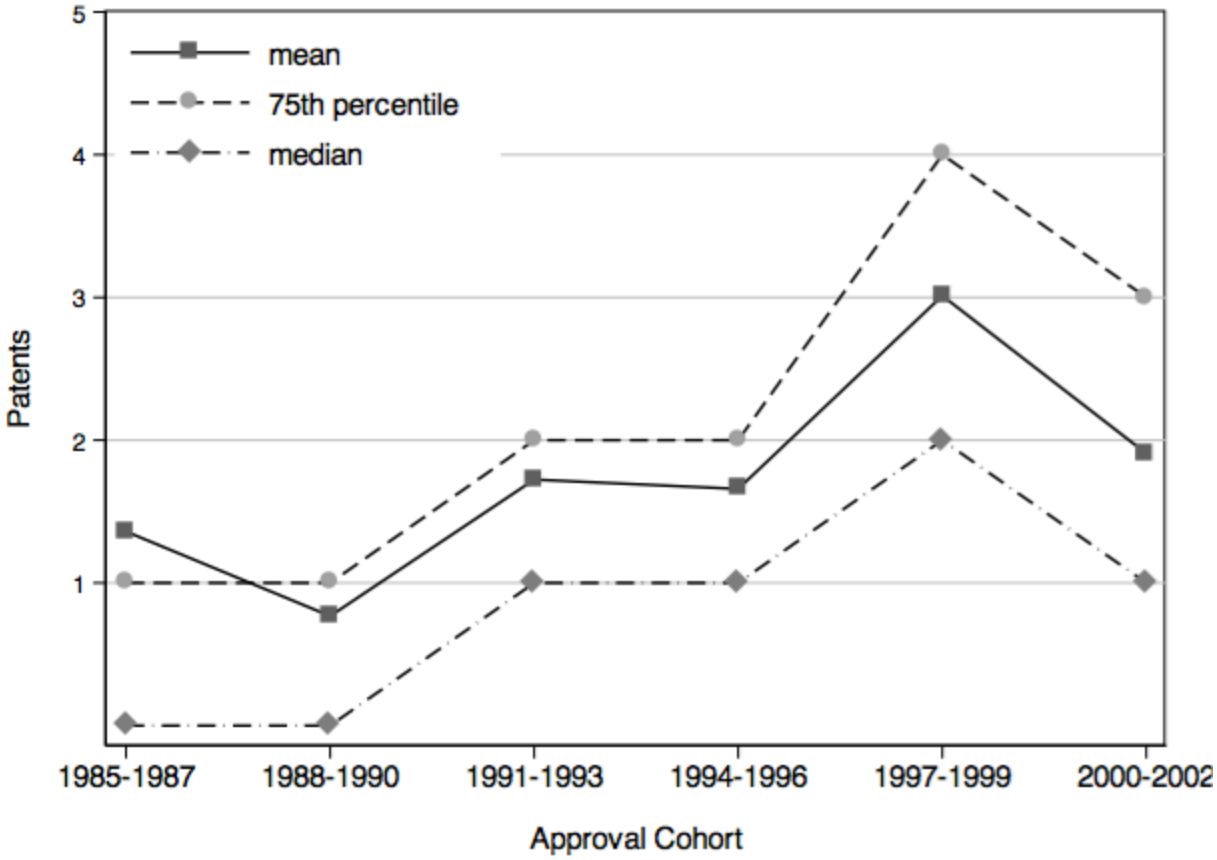

Table 1: Summary Statistics for 1992-1996 Approved NMEs

Variable	Mean	Std. Dev.	Min.	Max.	N
Generic Entry by 2011?	0.57	0.5	0	1	116
Generic in 15 years?	0.42	0.5	0	1	116
Natural Log Sales	17.78	2.3	8.27	22.37	116
Oral dosage form	0.52	0.5	0	1	116
Total OB Patents	2.84	2.41	1	11	116
Total non-OB Patents	1.74	2.58	0	15	116
Count of AI Patents	0.92	0.76	0	4	116
Count of non-AI Patents	1.92	2.34	0	11	116
Nominal Patent Term (Years) Based on OB Patents	16.44	5.12	1	30	116

Table 2: Effects of Sales, Drug Characteristics and Patent Characteristics on whether generic entry by 2011

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Natural Log Sales	0.0929*	0.0918*	0.0911*	0.0926*	0.0951*	0.0935*	0.0932*	0.0959*
	(0.0169)	(0.0184)	(0.0196)	(0.0179)	(0.0181)	(0.0174)	(0.0187)	(0.0175)
Oral dosage form	0.0197	0.0181	0.0176	0.0205	-0.00844	0.0225	0.0225	0.000215
	(0.103)	(0.105)	(0.105)	(0.103)	(0.109)	(0.106)	(0.107)	(0.110)
Total OB Patents		0.00326			-0.00783			
		(0.0159)			(0.0186)			
Count of AI Patents			0.0107					
			(0.0593)					
Count of non-AI Patents			0.00261					
			(0.0163)					
Nominal Patent Term				0.000429				
				(0.00741)				
Total non-OB Patents					0.0220			
					(0.0152)			
Total early OB Patents						-0.00574		-0.0141
						(0.0215)		(0.0234)
Total early AI Patents							-0.00251	
							(0.0696)	
Total early non-AI Patents							-0.00606	
							(0.0222)	
Total early non-OB Patents								0.0181
								(0.0170)
Constant	-0.934*	-0.924*	-0.918*	-0.937*	-0.974*	-0.938*	-0.936*	-0.973*
	(0.302)	(0.313)	(0.317)	(0.304)	(0.305)	(0.306)	(0.308)	(0.307)
F statistic	5.799	5.077	4.401	4.997	5.125	4.895	4.238	4.537
p value	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Observations	116	116	116	116	116	116	116	116

Notes: Sample comprises all new molecular entities (NMEs) approved between 1992 and 1996 with positive IMS sales five years post-approval, and at least one Orange Book patent. Log sales measured at five years after brand approval. Early patents are those issued within five years of brand approval. Generic entry defined as approval of a therapeutically equivalent abbreviated new drug application by December 2011.
Estimates are from ordinary least squares regressions. All models include indicators for therapeutic class and generic approval year. Heteroskedasticity-consistent standard errors in parentheses.
$+ \ p < 0.10$, $* \ p < 0.05$

Table 3: Effects of Sales, Drug Characteristics and Patent Characteristics on whether generic entry within 15 years

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Natural Log Sales	0.0587*	0.0552*	0.0585*	0.0574*	0.0567*	0.0598*	0.0612*	0.0617*
	(0.0182)	(0.0192)	(0.0191)	(0.0186)	(0.0195)	(0.0181)	(0.0183)	(0.0188)
Oral dosage form	0.117	0.112	0.114	0.122	0.101	0.122	0.122	0.104
	(0.102)	(0.104)	(0.105)	(0.103)	(0.111)	(0.106)	(0.107)	(0.115)
Total OB Patents		0.0106			0.00579			
		(0.0165)			(0.0197)			
Count of AI Patents			-0.0247					
			(0.0568)					
Count of non-AI Patents			0.0137					
			(0.0174)					
Nominal Patent Term				0.00226				
				(0.00787)				
Total non-OB Patents					0.00963			
					(0.0192)			
Total early OB Patents						-0.00914		-0.0157
						(0.0226)		(0.0251)
Total early AI Patents							-0.0240	
							(0.0660)	
Total early non-AI Patents							-0.00763	
							(0.0228)	
Total early non-OB Patents								0.0142
								(0.0189)
Constant	-0.634*	-0.601+	-0.626*	-0.653*	-0.623+	-0.641*	-0.650*	-0.669*
	(0.313)	(0.317)	(0.312)	(0.323)	(0.315)	(0.314)	(0.310)	(0.320)
F statistic	3.352	3.018	2.795	2.869	2.796	2.953	2.593	2.708
p value	0.005	0.006	0.008	0.009	0.008	0.007	0.013	0.010
Observations	116	116	116	116	116	116	116	116

Notes: Sample comprises all new molecular entities (NMEs) approved between 1992 and 1996 with positive IMS sales five years post-approval, and at least one Orange Book patent. Log sales measured at five years after brand approval. Early patents are those issued within five years of brand approval. Generic entry defined as approval of a therapeutically equivalent abbreviated new drug application within 15 years of approval.
Estimates are from ordinary least squares regressions. All models include indicators for therapeutic class and generic approval year. Heteroskedasticity-consistent standard errors in parentheses.
$+ \ p < 0.10$, $* \ p < 0.05$

Table 4: Summary Statistics for Drugs with First Generic Entry 2001-2010

Variable	Mean	Std. Dev.	Min.	Max.	N
Effective Market Life	12.1	3.35	5.74	23.09	123
Effective Market Life (Alt Measure)	12.62	3.28	5.74	23.1	115
Natural Log Sales	12.15	1.87	2.7	15.37	123
Oral dosage form	0.68	0.47	0	1	123
Total OB Patents	2.93	2.33	1	12	123
Total non-OB Patents	1.4	1.98	0	9	123
Count of AI Patents	0.99	0.71	0	4	123
Count of non-AI Patents	1.94	2.24	0	11	123
Nominal Patent Term (Years)	16.91	5.54	1.15	34.55	123

Table 5: Effects of Sales, Drug Characteristics and Patent Characteristics on Effective Market Life

	(1)	(2)	(3)	(4)	(5)
Natural Log Sales	-0.00176	-0.000340	-0.0225	-0.0719	0.00198
	(0.157)	(0.159)	(0.160)	(0.171)	(0.147)
Oral dosage form	-2.044*	-2.026*	-2.135*	-1.988*	-2.214*
	(0.656)	(0.680)	(0.693)	(0.655)	(0.690)
Total OB Patents		-0.0193			-0.102
		(0.142)			(0.140)
Count of AI Patents			0.402		
			(0.554)		
Count of non-AI Patents			-0.0499		
			(0.149)		
Nominal Patent Term (Years)				0.0925	
				(0.0570)	
Total non-OB Patents					0.338*
					(0.156)
Constant	14.78*	14.82*	14.78*	13.74*	14.68*
	(2.060)	(2.055)	(2.079)	(2.180)	(1.953)
F statistic	2.725	2.481	2.554	2.838	2.874
p value	0.00391	0.00676	0.00432	0.00209	0.00143
Observations	123	123	123	123	123
R-Squared	0.273	0.273	0.280	0.293	0.302

Notes: Sample comprises new molecular entities for which first generic entry occurred between 2001 and 2010. Each observation represents a drug. Effective market life is the time in years between brand approval and first generic entry. Nominal patent term is the time in years between brand approval and expiration of last patent. Estimates are from ordinary least squares regressions. Sales calculated in the year prior to generic entry

All models include indicators for therapeutic class and generic approval year. Heteroskedasticity-consistent standard errors in parentheses.

+ $p < 0.10$, * $p < 0.05$

Table 6: Effects of Sales, Drug Characteristics and Patent Characteristics on Alternate Measure of Effective Market Life

	(1)	(2)	(3)	(4)	(5)
Natural Log Sales	0.0670	0.0662	0.0410	-0.0130	0.0726
	(0.153)	(0.155)	(0.156)	(0.167)	(0.143)
Oral dosage form	-1.946*	-1.966*	-2.090*	-1.880*	-2.109*
	(0.641)	(0.672)	(0.700)	(0.634)	(0.687)
Total OB Patents		0.0205			-0.0623
		(0.150)			(0.152)
Count of AI Patents			0.546		
			(0.603)		
Count of non-AI Patents			-0.00926		
			(0.154)		
Nominal Patent Term (Years)				0.108+	
				(0.0577)	
Total non-OB Patents					0.319+
					(0.165)
Constant	14.14*	14.08*	13.95*	12.91*	13.88*
	(2.034)	(2.017)	(2.052)	(2.169)	(1.910)
F statistic	2.401	2.224	2.198	2.867	2.496
p value	0.0111	0.0161	0.0151	0.00206	0.00560
Observations	115	115	115	115	115
R-Squared	0.243	0.243	0.253	0.272	0.271

Notes: Sample comprises new molecular entities for which first generic entry occurred between 2001 and 2010. Each observation represents a drug. This alternative measure of effective market life is the time in years between brand approval and first generic launch. Drugs with generic approvals but no launches are dropped.
Nominal patent term is the time in years between brand approval and expiration of last patent. Estimates are from ordinary least squares regressions. Sales calculated in the year prior to generic entry
All models include indicators for therapeutic class and generic approval year. Heteroskedasticity-consistent standard errors in parentheses.
$+ \ p < 0.10$, $* \ p < 0.05$

Table 7: Litigation By Patent Type

	No Litigation Freq/Row Pct	Litigation Freq/Row Pct	Total Freq/Row Pct
Non-AI Patent	73	86	159
	45.91	54.09	100.00
AI Patent	10	21	31
	32.26	67.74	100.00
Total	83	107	190
	43.68	56.32	100.00

Table 8: Litigation Outcomes By Patent Type

	Brand Freq/Row Pct	Generic Freq/Row Pct	Total Freq/Row Pct
Non-AI Patent	9	45	54
	16.67	83.33	100.00
AI Patent	11	2	13
	84.62	15.38	100.00
Total	20	47	67
	29.85	70.15	100.00