NOTE

HOW MANY PATENTS DOES IT TAKE TO MAKE A DRUG? FOLLOW-ON PHARMACEUTICAL PATENTS AND UNIVERSITY LICENSING

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* Yale Law School, J.D. expected 2011; Cornell University, Ph.D. 2008; Swarthmore College, B.A. 2002. I am indebted to Bhaven Sampat for sharing his *Orange Book* patent data and for providing valuable suggestions as this work unfolded. I am also very grateful to John J. Donohue, III and Christopher L. Griffin, Jr. for their guidance on my empirical analyses, and to Amy Kapczynski for her thoughtful comments. Finally, I would like to thank the careful editors at the *Michigan Telecommunications and Technology Law Review*.

INTRODUCTION

The pharmaceutical industry is the poster child for a strong patent system.[1] Drug companies bear the high costs of obtaining approval from the Food and Drug Administration (FDA) only because they can then charge high prices for patented drugs without fear of generic competition.[2] As described by Professors Dan Burk and Mark Lemley, drugs are also special because of the low number of patents per product: "In some industries, such as chemistry and pharmaceuticals, a single patent normally covers a single product. Much conventional wisdom in the patent system is built on the unstated assumption of such a one-to-one correspondence."[3] Although many have repeated this one-patent, one-drug assumption,[4] there has been little empirical analysis of how many patents actually protect each drug.

In fact, most small-molecule drugs are protected by multiple patents. The average was nearly 3.5 patents per drug in 2005, with over five patents per drug for the best-selling pharmaceuticals; these numbers have increased over time.[5] This Note contains a detailed empirical examination of how many patents cover FDA-approved small-molecule drugs,

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1. *See, e.g.*, WILLIAM M. LANDES & RICHARD A. POSNER, THE ECONOMIC STRUCTURE OF INTELLECTUAL PROPERTY LAW 316 (2003) ("[T]he strongest case for patents in something like their present form is said to be found in a subset of the drug industry."); Amy Kapczynski et al., *Addressing Global Health Inequities: An Open Licensing Approach for University Innovations*, 20 BERKELEY TECH. L.J. 1031, 1044–45 (2005) ("Many who accept these premises [that strong patents reduce innovation and welfare] nonetheless consider the pharmaceutical sector an exception.").

2. Alternative funding for pharmaceutical innovation, such as prize systems, may lead to better health outcomes. *See* Kapczynski et al., *supra* note 1, at 1045 & nn.57–58. Currently, however, patents are the main mechanism to promote drug innovation.

3. Dan L. Burk & Mark A. Lemley, *Policy Levers in Patent Law*, 89 VA. L. REV. 1575, 1590 (2003).

4. *See, e.g.*, Graeme B. Dinwoodie & Rochelle C. Dreyfuss, *Diversifying Without Discriminating: Complying with the Mandates of the TRIPS Agreement*, 13 MICH. TELECOMM. & TECH. L. REV. 445, 445 (2007) ("In some fields, like pharmaceuticals, the [patent-to-product] ratio is close to one (one patent covers one product)."); Mark A. Lemley, *Ten Things To Do About Patent Holdup of Standards (and One* Not *To)*, 48 B.C. L. REV. 149, 150 (2007) ("[G]enerally, one patent covers one drug."); George A. Vinyard, Address at the Michigan Telecommunications and Technology Law Review Symposium: Law, Policy and the Convergence of Telecommunications and Computer Technologies (Mar. 9, 2001), *available at* http://www.mttlr.org/html/symposia/convergence/wireless.html ("A lot of patent thinking appears to be based on a fairly simple commercial model, like pharmaceuticals where there's one patent, one product, one-to-one coverage, that's it.").

5. Small-molecule drugs have relatively simple chemical structures and are regulated under the Hatch-Waxman Act, which requires pharmaceutical companies to list the patents that cover each drug. *See infra* Part I.B. There is no similar patent data for more complicated biologic drugs, but pharmaceutical companies will soon be required to provide this data under the recent healthcare reform bill. Patient Protection and Affordable Care Act, Pub. L. No. 111-148, § 7002, 124 Stat. 119, 811 (2010) (to be codified in scattered sections of 42 U.S.C.).

what factors influence the number of patents, and the implications of having multiple patents on a drug.[6]

In particular, "follow-on" patents have important implications for the growing number of universities and other public-sector research institutions that want to make their patented medical technologies accessible in developing countries.[7] For example, if a university chooses not to patent a new drug molecule in India but subsequently licenses its U.S. patent on that molecule to a pharmaceutical company that files a follow-on method-of-treatment patent in India, then Indian generic manufacturers will be unable to produce the drug.[8] These results are important for the ongoing debate about public-sector patenting.[9] The widespread prevalence of follow-on patents also has implications beyond the university context, since these patents generally extend the patent life of a drug.

This Note proceeds in four Parts. Part I examines the role of patents in drug development and the regulatory environment under the Hatch-Waxman Act. Part II discusses ways in which follow-on patents can impede socially responsible licensing efforts by universities and other public-sector institutions. Part III presents an empirical analysis of drug patent data, which shows that the number of patents per drug has increased over time, and examines factors that have influenced this trend. The data also reveal that drugs with public-sector patents are more likely to have follow-on patents than drugs without public-sector patents. However, because many of these follow-on patents are additional public-sector patents, the drugs with public-sector patents are actually less likely to have private-sector follow-on patents. Finally, Part IV describes a table of detailed patent information for eighteen recently approved drugs with both public- and private-sector patents and discusses the implications of these results for university patenting and licensing. Over half of public-sector drugs still have private-sector patents, so public-sector institutions that want their drugs to be generically produced for patients in developing countries will need to request licensing terms that prevent private-sector patents from blocking patient access.

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6. This Note is the first to provide this detailed empirical analysis, but others have noted that the one-patent, one-drug assumption does not reflect reality. *See* FED. TRADE COMM'N, GENERIC DRUG ENTRY PRIOR TO PATENT EXPIRATION: AN FTC STUDY 39–40 (2002), *available at* http://www.ftc.gov/os/2002/07/genericdrugstudy.pdf (noting that brand-name companies are sometimes suing over three or more patents for high-earning drugs); C. Scott Hemphill & Bhaven N. Sampat, Generic Drug Challenges Prior to Patent Expiration 14 (Mar. 1, 2010) (unpublished manuscript) (on file with author) (finding that the number of patents per drug has been increasing over time).

7. For the purposes of this Note, a "follow-on patent" is defined as any patent beyond the initial patent on a drug. For example, a drug with three patents has two follow-on patents. A "public-sector" institution is a university, institute, hospital, or government.

8. *See* Kapczynski et al., *supra* note 1, at 1084 & n.253.

9. *See infra* notes 54–60 and accompanying text.

I. THE ROLE OF PATENTS IN DRUG DEVELOPMENT

A. *Patents and the Economics of Drug Development*

Bringing a new drug to market is expensive. The pharmaceutical industry group, the Pharmaceutical Research and Manufacturers of America (PhRMA), claims that the research and development (R&D) cost per approved drug was $1.3 billion in 2005,[10] up from $802 million in 2001.[11] The accuracy of this industry-funded research is highly contested.[12] Whether the exact figure is $100 million or $1 billion, however, it is clear that the cost of research and testing is very high.

After one pharmaceutical company has undertaken the expense of discovering a drug and proving its efficacy and safety through clinical trials, it is comparatively inexpensive for a generic company to enter the market; one estimate placed the entry cost in the 1990s at $603,000.[13] Because of the high ratio of R&D costs to imitation costs, there would be little incentive for innovator pharmaceutical companies to develop new drugs in the absence of effective legal protection against imitators.[14] The patent system provides one such form of protection.[15]

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10. PHARM. RESEARCH & MFRS. OF AM., PHARMACEUTICAL INDUSTRY PROFILE, at inside front cover (2010) (citing Joseph A. DiMasi & Henry G. Grabowski, *The Cost of Biopharmaceutical R&D: Is Biotech Different?*, 28 MANAGERIAL & DECISION ECON. 469 (2007)), *available at* http://www.phrma.org/sites/phrma.org/files/attachments/Profile_2010_FINAL.pdf.

11. *Id.* (citing Joseph A. DiMasi, Ronald W. Hansen & Henry G. Grabowski, *The Price of Innovation: New Estimates of Drug Development Costs*, 22 J. HEALTH ECON. 151 (2003)).

12. *See, e.g.*, MARCIA ANGELL, THE TRUTH ABOUT THE DRUG COMPANIES: HOW THEY DECEIVE US AND WHAT TO DO ABOUT IT 37–46 (2004) (suggesting that the actual average development cost is under $100 million); Richard G. Frank, Editorial, *New Estimates of Drug Development Costs*, 22 J. HEALTH ECON. 325, 325 (2003) (stating that the $802 million estimates "have been a matter of heated debate since they were first made public in 2001"); Donald W. Light, *Misleading Congress About Drug Development*, 32 J. HEALTH POL. POL'Y & L. 895, 897–900 (2008) (reviewing CONG. BUDGET OFFICE, RESEARCH AND DEVELOPMENT IN THE PHARMACEUTICAL INDUSTRY (2006)) (criticizing DiMasi, Hansen, and Grabowski's sample as "nonrandom and small" and "unverifiable industry data," and arguing that their estimate of development costs may be off by a factor of ten); Donald W. Light, *Reply to DiMasi, Hansen, and Grabowski*, 33 J. HEALTH POL. POL'Y & L. 325 (2008) (rebutting DiMasi, Hansen, and Grabowski's criticisms of Light's criticisms of their work); F.M. Scherer, *The Pharmaceutical Industry—Prices and Progress*, 351 NEW ENG. J. MED. 927, 928 (2004) (noting that the $802 million estimate "must be regarded with caution" because the sample came from only ten companies, "[o]nly about half the estimated price tag entailed actual out-of-pocket costs," and the sample "placed a disproportionate emphasis on drugs for chronic diseases, which require extensive testing to identify long-term effects").

13. David Reiffen & Michael R. Ward, *Generic Drug Industry Dynamics*, 87 REV. ECON. & STAT. 37, 47 (2005).

14. *See* Burk & Lemley, *supra* note 3, at 1616–17.

15. Patents are not the only way to provide incentives for new medical technologies; recent proposals advocate de-linking research and development costs from manufacturing costs by rewarding a new innovation based on its health impact. *See* Medical Innovation Prize

Empirical studies have repeatedly found that while patents are surprisingly unimportant for appropriating returns on R&D in most industries, they are very important in the pharmaceutical industry. One study of 100 randomly selected firms found that patents were "essential for the development or introduction of 30 percent or more of the inventions in only two industries—pharmaceuticals and chemicals."[16] Based on 650 completed questionnaires from industrial research managers, Levin and his colleagues found that "[i]n only one industry, drugs, were product patents regarded by a majority of respondents as strictly more effective than other means of appropriation," and they described pharmaceuticals as "one of the few [industries] in which patents really do seem to matter."[17] In a later survey of R&D managers with 1478 respondents, Cohen, Nelson, and Walsh similarly found that the pharmaceutical industry was one of the few places "where patents are effective."[18]

Although these surveys are over ten years old,[19] the importance of patents to the pharmaceutical industry has not abated.[20] Pharmaceutical companies spend more money on lobbying than any other industry—over $200 million in 2007—much of which is devoted to maintaining a strong patent system.[21] Part of this effort is focused on general patent

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Act of 2007, S. 2210, 110th Cong. (2007); AIDAN HOLLIS & THOMAS POGGE, THE HEALTH IMPACT FUND: MAKING NEW MEDICINES ACCESSIBLE FOR ALL (2008), *available at* http://www.yale.edu/macmillan/igh/; Barbados, Bolivia, Suriname & Bangladesh, A Prize Fund To Support Innovation and Access for Donor Supported Markets (Apr. 15, 2009), http://www.who.int/phi/Bangladesh_Barbados_Bolivia_Suriname_DonorPrize.pdf.

16. Edwin Mansfield, *Patents and Innovation: An Empirical Study*, 32 MGMT. SCI. 173, 174 (1986).

17. Richard C. Levin et al., *Appropriating the Returns from Industrial Research and Development*, 1987 BROOKINGS PAPERS ON ECON. ACTIVITY 783, 796, 824.

18. Wesley M. Cohen, Richard R. Nelson & John P. Walsh, *Protecting Their Intellectual Assets: Appropriability Conditions and Why U.S. Manufacturing Firms Patent (or Not)* 23, 32 tbl.1 (Nat'l Bureau of Econ. Research, Working Paper No. 7552, 2000), *available at* http://www.nber.org/papers/w7552.pdf. Cohen and his colleagues also found that "in *no* industry are patents identified as the most effective appropriability mechanism"—other methods like secrecy and lead time are more important. *Id.* at 9 (emphasis added).

19. Although there are no more recent surveys that include the pharmaceutical industry, the 2008 Berkeley Patent Survey of 1332 high technology start-up companies provides some "nuanced and multi-faceted" results on the utility of patents for entrepreneurs. *See* Stuart J.H. Graham, Robert P. Merges, Pam Samuelson & Ted Sichelman, *High Technology Entrepreneurs and the Patent System: Results of the 2008 Berkeley Patent Survey*, 24 BERKELEY TECH. L.J. 1255, 1262 (2010).

20. *See* Jay P. Kesan, *Transferring Innovation*, 77 FORDHAM L. REV. 2169, 2195 (2009) (noting that the comparative value of each patent is much higher in the life sciences than in engineering fields and that patents are not important for technology transfer in most fields other than pharmaceuticals and biotechnology).

21. *See* Jay P. Kesan & Andres A. Gallo, *The Political Economy of the Patent System*, 87 N.C. L. REV. 1341, 1353, 1359–61 (2009).

reform,[22] but pharmaceutical manufacturers also operate within a complex regulatory environment under the FDA, which "blur[s] the functional distinction between drug regulation and patents."[23] This legislative regime is described in the following section.

B. *FDA Regulation of Drug Patents and the Hatch-Waxman Act*

The Hatch-Waxman Act of 1984[24] is a legislative compromise between large brand-name companies, who disliked losing part of their patent term to long FDA approval periods, and generic companies, who disliked having to re-prove the safety and efficacy of drugs that were already on the market.[25] The resulting regulatory regime confers some additional market protections for new drugs.

Under the Hatch-Waxman regime, a brand-name company seeking FDA approval for a new drug must file a new drug application (NDA).[26] In addition to detailed information about the properties of the drug, the application must include "the patent number and the expiration date of any patent which claims the drug . . . or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted," and this information must be amended as new patents are issued.[27] After the drug is approved, the FDA must make this list public.[28] The FDA publication containing new drug information is known as the *Orange Book*, and it may be searched freely online.[29]

The FDA is not required to review patents before listing them,[30] which has led to concerns about abuse of the *Orange Book* by brand-name pharmaceutical companies. Professor Rebecca Eisenberg has summarized the process of "evergreening" drug patents:

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22. *See, e.g.*, Press Release, Pharm. Research & Mfrs. of Am., PhRMA Statement on Patent Reform Act of 2009 (Mar. 3, 2009), *available at* http://www.phrma.org/news_room/press_releases/phrma_statement_on_patent_reform_act_of_2009 ("[T]he bill would reduce the value of the patents that are the lifeblood of America's innovative business sectors, which depend on intellectual property protection.").

23. Rebecca S. Eisenberg, *The Role of the FDA in Innovation Policy*, 13 MICH. TELECOMM. TECH. L. REV. 345, 357 (2007).

24. Drug Price Competition and Patent Term Restoration (Hatch-Waxman) Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (codified in scattered sections of 15, 21, and 35 U.S.C.).

25. In addition to the needless expense, there are ethical problems with giving sick patients a placebo when the efficacy of the test drug is already proven.

26. *See* 21 U.S.C. § 355(b)(1) (2006); 21 C.F.R. § 314 (2009).

27. 21 U.S.C. § 355(b)(1); *accord* 21 C.F.R. § 314.53 (providing more details about which patents must be submitted).

28. 21 U.S.C. § 355(b)(1); 21 C.F.R. § 314.53(e).

29. OFFICE OF GENERIC DRUGS, FDA, ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS (30th ed. 2010) [hereinafter ORANGE BOOK], *available at* http://www.fda.gov/cder/ob/default.htm.

30. Apotex, Inc. v. Thompson, 347 F.3d 1335, 1349 (Fed. Cir. 2003).

> In recent years drug innovators have sought to prolong their effective periods of patent protection through various "evergreening" strategies that add new patents to their quivers as old ones expire. Examples include patents on "metabolites" (i.e., the products into which drugs are transformed in a patient's body); patents on intermediate products used in producing drugs; patents on new uses for drugs; and patents on new formulations or preparations. Some innovating firms have succeeded in getting such patents issued by the PTO, and in using them to defer FDA approval of generic products for years pending resolution of patent infringement claims. The industry's track record in actually winning these infringement claims, however, has been considerably worse . . . .[31]

In particular, commentators have suggested that many of these follow-on patents may be rendered obvious in light of *KSR v. Teleflex*.[32]

Once the FDA has approved an NDA, a generic company may then seek FDA approval using an abbreviated new drug application (ANDA), in which it must show that the generic is "bioequivalent to the listed drug."[33] It does not need to re-prove the safety and efficacy of the drug. The generic company also must provide a certification for each patent listed in the *Orange Book*.[34] If the company seeks FDA approval prior to patent expiration, it files a "paragraph IV" certification, claiming that "such patent is invalid or will not be infringed."[35] The first generic company to receive FDA approval after a paragraph IV certification receives 180 days of market exclusivity,[36] providing a significant incentive for generic companies to challenge patents.

The brand-name company may then file a patent infringement suit within forty-five days, which provides a thirty-month stay before the FDA will approve the generic, effectively giving the brand-name

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31. Eisenberg, *supra* note 23, at 354 (footnotes omitted). For a primer on how to use patent filings to extend the patent life of a drug, see Tamsen Valoir, *Six Methods of Preserving Market Exclusivity*, INTELL. PROP. & TECH. L.J., Nov. 2006, at 12, 14.

32. KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, 415 (2007) (finding a car pedal design obvious and rejecting the Federal Circuit's "rigid approach" to obviousness in favor of "an expansive and flexible" approach); *see, e.g.*, Rebecca S. Eisenberg, *Pharma's Nonobvious Problem*, 12 LEWIS & CLARK L. REV. 375, 423 (2008) ("The practical effect [of the Federal Circuit's post-*KSR* cases] is to make it more difficult to obtain evergreening patents on new versions of successful products . . . ."); Michael Enzo Furrow, *Pharmaceutical Patent Life-Cycle Management After* KSR v. Teleflex, 63 FOOD & DRUG L.J. 275, 277 (2008) ("[T]he post-*KSR* non-obviousness standard will likely excise some 'secondary' pharmaceutical inventions from the realm of patentability.").

33. 21 U.S.C. § 355(j)(2)(A)(iv); *accord* 21 C.F.R. § 314.94(a)(7).

34. 21 U.S.C. § 355(j)(2)(A)(vii); 21 C.F.R. § 314.94(a)(12).

35. 21 U.S.C. § 355(j)(2)(A)(vii)(IV); *accord* 21 C.F.R. § 314.94(a)(12)(i)(A)(4).

36. 21 U.S.C. § 355(j)(5)(B)(iv); 21 C.F.R. § 314.107(c).

company an additional form of exclusivity.[37] Under the original 1984 provision, brand-name companies could obtain multiple thirty-month stays, which led to concerns about abuse. For example, a Federal Trade Commission (FTC) report noted eight instances in which brand-name companies listed additional *Orange Book* patents after an ANDA was filed, many of which "do not appear to claim the approved drug product or an approved use of the drug."[38] This provision was limited to one thirty-month stay in 2003, first by executive action and then as part of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003.[39]

Another form of exclusivity granted by the Hatch-Waxman Act is data exclusivity. This prevents generic companies from submitting an ANDA within five years of the approval of a drug, "no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application," and for three years after approval of a drug "if such application contains reports of new clinical investigations."[40]

Finally, the Hatch-Waxman Act also allows pharmaceutical companies to obtain a patent term extension to extend the life of one patent listed in the *Orange Book* by up to five years.[41] Only one patent per drug may be extended,[42] and extensions are granted only for "the first permitted commercial marketing or use of the product,"[43] meaning that a patent owner cannot extend a patent on a drug that is merely a new formulation of an old "product."[44] A patent term extension is not automatic; the patent owner must apply for it in accordance with a set of detailed rules.[45]

II. Follow-On Patents and Socially Responsible Licensing

While follow-on patents can delay generic entry, they have even more important implications for drugs arising from public research. As

37. 21 U.S.C. § 355(j)(5)(B)(iii); 21 C.F.R. § 314.107(b)(3). The FDA may approve the drug sooner if the court happens to reach a final decision on the patents at issue before the thirty-month stay expires. 21 C.F.R. § 314.107(b)(3)(ii).

38. Fed. Trade Comm'n, *supra* note 6, at 40.

39. Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub. L. No. 108-173, § 1101, 117 Stat. 2066, 2448–57; *see also* Eisenberg, *supra* note 23, at 358 n.54, 366 n.88.

40. 21 U.S.C. § 355(c)(3)(E)(ii)-(iii), (j)(5)(F)(ii)-(iv); *accord* 21 C.F.R. § 314.108.

41. 35 U.S.C. § 156 (2006). A patent can only be extended if it has not expired and if it has not previously been extended. *Id.* § 156(a)(1)-(2).

42. *Id.* § 156(b).

43. *Id.* § 156(a)(5).

44. The meaning of "product" is disputed. *See infra* note 84 and accompanying text.

45. *See* 35 U.S.C. § 156(a)(3), (d)(1)-(4) (listing application deadlines and required contents).

described in this Part, many universities and public-sector institutions have important drug patents, but efforts to license these patents to promote the public interest can be derailed by private-sector follow-on patents.

Since the Bayh-Dole Act of 1980,[46] universities and other recipients of federal funds have been able to patent and exclusively license their discoveries "to promote the utilization of inventions arising from federally supported research."[47] Federally funded medical research had long provided the foundations for many new drugs without needing patents to create incentives for these innovations.[48] However, the Bayh-Dole Act has resulted in direct institutional ownership of parts of the intellectual property that protects many new drugs.[49]

To justify granting these private patent rights for government-sponsored inventions, one cannot use the typical innovation incentive of patents, because academic researchers have been innovating long before the Bayh-Dole Act and are primarily motivated by a desire for prestige.[50] Instead, Bayh-Dole patents typically are justified under commercialization theory—the idea that companies need exclusive patent rights to bring an invention to market.[51] Commercialization theory is not appropriate for many industries,[52] but exclusive rights may be needed in the pharmaceutical industry because of the high cost of FDA approval and low cost of imitation.[53]

Still, granting exclusive patent rights may lead to monopoly pricing and the resulting inefficiencies, depending on the availability of

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46. Bayh-Dole Act of 1980, 35 U.S.C. §§ 200–212 (2006).

47. *Id.* § 200. Other access-oriented goals of the Bayh-Dole Act include "promot[ing] *free competition* and enterprise without unduly encumbering future research" and "promot[ing] the commercialization and *public availability* of inventions made in the United States." *Id.* (emphasis added); *cf.* Kesan, *supra* note 20, at 2176–77 (discussing conflicting views of the purpose of the Bayh-Dole Act).

48. *See, e.g.*, Richard B. Thompson, *Foundations for Blockbuster Drugs in Federally Sponsored Research*, 15 FASEB J. 1671 (2001) (discussing the federally funded research foundations for Zocor, Pravachol, and Lipitor, none of which have patents from public-sector institutions).

49. *See* Bhaven N. Sampat, *Academic Patents and Access to Medicines in Developing Countries*, 99 AM. J. PUB. HEALTH 9, 11–14 (2009) (describing seventy-two drugs with patents owned by thirty-five public-sector institutions).

50. *See* Mark A. Lemley, *Are Universities Patent Trolls?*, 18 FORDHAM INTELL. PROP. MEDIA & ENT. L.J. 611, 621 (2008); Arti Kaur Rai, *Regulating Scientific Research: Intellectual Property Rights and the Norms of Science*, 94 NW. U. L. REV. 77, 92 (1999).

51. *See* Lemley, *supra* note 50, at 621; Rai, *supra* note 50, at 97–99.

52. *See* Lisa Larrimore Ouellette, Comment, *Addressing the Green Patent Global Deadlock Through Bayh-Dole Reform*, 119 YALE L.J. 1727, 1731–32 (2010) (citing references to show why commercialization theory is not appropriate for engineering fields and arguing that universities should not be allowed to seek patents or exclusive licenses for most green technologies).

53. *See supra* notes 10–14 and accompanying text.

substitutes.[54] Furthermore, most university technology transfer officers—who have different motivations from individual researchers—are not focused on increasing public access to public-sector inventions.[55] A recent study found that "university technology transfer activities continue to be predominately patent-centric and revenue-driven with a single-minded focus on generating licensing income and obtaining reimbursement for legal expenses."[56] Current Bayh-Dole patenting and licensing practices have thus been criticized for creating unnecessary increases in consumer prices[57] and for creating patent hold-ups and a patent "anticommons."[58]

The access-oriented goals of the Bayh-Dole Act would be fulfilled best if universities and other recipients of federal research grants only granted exclusive patent licenses to the extent necessary for commercialization.[59] Scholars and advocates have urged public-sector institutions to adopt more socially responsible patenting and licensing policies that follow this principle of promoting access, particularly among those suffering from global health inequalities.[60] A small but growing number of institutions are focusing on this goal, as discussed in the remainder of this Part.

Developing countries bear a disproportionate fraction of the world's disease burden. Millions of people die each year from preventable and

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54. *See* LANDES & POSNER, *supra* note 1, at 300.

55. *See* Ouellette, *supra* note 52, at 1733 & n.34.

56. Kesan, *supra* note 20, at 2169. Kesan notes that most university technology transfer offices have failed to break even, so they are not particularly successful at this revenue focus. *See id.* at 2180 & n.64.

57. *See, e.g.*, Clifton Leaf, *The Law of Unintended Consequences*, FORTUNE, Sept. 19, 2005, at 250, *available at* http://money.cnn.com/magazines/fortune/fortune_archive/2005/09/19/8272884/index.htm.

58. *See* Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCIENCE 698, 698 (1998); Lemley, *supra* note 50, at 615–19; Arti K. Rai & Rebecca S. Eisenberg, *Bayh-Dole Reform and the Progress of Biomedicine*, 66 LAW & CONTEMP. PROBS. 289, 295–303 (2003); Anthony D. So et al., *Is Bayh-Dole Good for Developing Countries? Lessons from the US Experience*, 6 PLOS BIOLOGY 2078, 2080 (2008). The anticommons and hold-up problems both stem from transaction costs. An anticommons is the result of patents on basic research impeding future research, and a patent hold-up occurs when a patent-holder impedes development by demanding royalties.

59. For example, the National Institutes of Health (NIH) has stated that for genomic inventions, "grant recipients' responsibilities under the Bayh-Dole Act" include pursuing non-exclusive licensing "[w]henever possible" and narrowly tailored exclusive licenses only when necessary "with the goal of promoting [federally funded inventions'] utilization, commercialization, and public availability." Best Practices for the Licensing of Genomic Inventions: Final Notice, 70 Fed. Reg. 18,413, 18,413–15 (Apr. 11, 2005).

60. *See, e.g.*, Kapczynski et al., *supra* note 1; Beirne Roose-Snyder & Megan K. Doyle, *The Global Health Licensing Program: A New Model for Humanitarian Licensing at the University Level*, 35 AM. J.L. & MED. 281 (2009); Andrew Gray, *University Technology Transfer*, U. ALLIED FOR ESSENTIAL MEDICINES (Sept. 12, 2009, 17:07), http://essentialmedicine.org/projects/university-technology-transfer.

treatable diseases, in part due to the high cost of patented medicines.[61] Because pharmaceutical revenues from developing countries are small,[62] socially responsible licensing advocates argue that the potential profits from those countries are not necessary to promote commercialization.[63] Universities could thus pursue a market-segmentation strategy, allowing pharmaceutical companies to recoup their development costs in high-income countries while allowing generic competition in low- and middle-income countries.

Universities are able to influence global health. For example, in 1990 Yale patented the use of the drug stavudine (d4T) to treat HIV and granted an exclusive license to Bristol-Myers Squibb.[64] Under the trade name Zerit, stavudine became a key drug for treating HIV. With a cost of over $1600 per year, however, it was inaccessible to most patients in developing countries.[65] Médecins Sans Frontières (MSF) wanted to distribute stavudine in South Africa. An Indian manufacturer offered to supply the drug for $40 per year, but MSF was unable to accept because Yale had patented stavudine in South Africa. With the help of Yale Law students Amy Kapczynski (now a law professor) and Marco Simons, MSF approached Yale, which began negotiating with Bristol-Myers Squibb.[66] After the issue was publicized in the *New York Times*,[67] Bristol-Myers Squibb announced that it would not enforce the stavudine patent in South Africa and that it would sell Zerit in sub-Saharan Africa for $55 per year.[68]

Out of this student movement at Yale, the group Universities Allied for Essential Medicines (UAEM) was formed to encourage universities to consider global health inequalities when they initially patent and

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61. *See* Kapczynski et al., *supra* note 1, at 1032; Roose-Snyder & Doyle, *supra* note 60, at 281.

62. *See* PHARM. RESEARCH & MFRS. OF AM., *supra* note 10, at 51 tbl.9 (reporting that for PhRMA members in 2008, Africa constituted 0.5% of sales, China constituted 0.9%, India constituted 0.2%, and all of the Americas except the United States and Canada constituted 3.8%).

63. *See* Kapczynski et al., *supra* note 1, at 1088–89, 1098–1100; Roose-Snyder & Doyle, *supra* note 60, at 285–98; UNIVS. ALLIED FOR ESSENTIAL MEDS., GLOBAL ACCESS LICENSING FRAMEWORK 4–5 (2010), *available at* http://essentialmedicine.org/sites/default/files/archive/Framework%20V2.doc.

64. *See* Kapczynski et al., *supra* note 1, at 1035.

65. *See id.* at 1032, 1034.

66. Daryl Lindsey, *Amy and Goliath*, SALON (May 1, 2001), http://www.salon.com/news/feature/2001/05/01/aids.

67. *See* Donald G. McNeil Jr., *Yale Pressed To Help Cut Drug Costs in Africa*, N.Y. TIMES, Mar. 12, 2001, at A3; William Prusoff, Op-Ed, *The Scientist's Story*, N.Y. TIMES, Mar. 19, 2001, at A19.

68. *See, e.g.*, Kapczynski et al., *supra* note 1, at 1036; Lindsey, *supra* note 66.

license new medicines.[69] In response to this movement, the Association of University Technology Managers (AUTM) and a number of universities have endorsed two licensing policy statements that address global health.

In 2007, a group of eleven universities and the Association of American Medical Colleges (AAMC) signed a statement—*Nine Points To Consider in Licensing University Technologies*—describing licensing practices to ensure that the "core values" of universities are "maintained to the fullest extent possible in all technology transfer agreements."[70] The signatories believe that "[u]niversities have a social compact with society" that gives them "a responsibility . . . to share the fruits" of their inventions with "the world's poor."[71] The final suggestion states: "Universities should strive to construct licensing arrangements in ways that ensure that these underprivileged populations [in developing countries and other underserved populations] have low- or no-cost access to adequate quantities of these medical innovations."[72] This statement now has seventy-four signatories, including AUTM.[73]

More recently, AUTM, the NIH, the Centers for Disease Control and Prevention (CDC), and nineteen universities and hospitals have endorsed the 2009 *Statement of Principles and Strategies for the Equitable Dissemination of Medical Technologies* (*Statement of Principles and Strategies*).[74] This policy statement argues that "[u]niversities have a fundamental role in fostering public health" and lists "strategies that promote the availability of health-related technologies in developing countries for essential medical care," including "not patenting in developing countries," "filing and abandoning patents," and "[e]arly publication and wide dissemination of results" to create prior art that would preclude patenting.[75] UAEM praised this new policy but expressed

69. *See History*, U. Allied for Essential Medicines, http://essentialmedicine.org/about-us/history (last visited June 22, 2010).

70. Cal. Inst. of Tech. et al., In the Public Interest: Nine Points To Consider in Licensing University Technology 1 (2007), *available at* http://www.autm.net/Nine_Points_to_Consider.htm.

71. *Id.* at 8.

72. *Id.*

73. *Endorse the Nine Points To Consider*, Ass'n U. Tech. Managers, http://www.autm.net/source/NinePoints/ninepoints_endorsement.cfm (last visited June 20, 2010).

74. *Endorse the Statement of Principles and Strategies for the Equitable Dissemination of Medical Technologies*, Ass'n U. Tech. Managers, http://www.autm.net/endorse (last visited June 20, 2010). The full text of the statement is available on AUTM's website. Ass'n of Univ. Tech. Managers et al., Statement of Principles and Strategies for the Equitable Dissemination of Medical Technologies (2009), *available at* http://www.autm.net/Content/NavigationMenu/TechTransfer/GlobalHealth/statementofprincliples.pdf.

75. Ass'n of Univ. Tech. Managers et al., *supra* note 74, at 1–2.

concern that these strategies would be insufficient to ensure access if pharmaceutical companies file follow-on patents:

> Although the signatories . . . have made the highly commendable commitment that university intellectual property should not become a barrier to patient access to essential health-related technologies, the commitment [to access] will be meaningless unless it allows patients to have access to the final end product. To ensure access, universities must also ensure that their licensees' intellectual property does not become such a barrier. If universities do not adopt such pro-active measures, then a licensee may preclude access by filing follow-on product, process, or use patents, utilizing trade secret protection, or exercising data exclusivity.[76]

There has been no empirical analysis, however, of how significant this problem might be. How often do university drugs have follow-on patents, and are follow-on patents more or less likely on university drugs than on drugs without public-sector contributions? The following Part examines these questions.

III. Empirical Analysis of Pharmaceutical Patent Data

A. *Data Sources and Summary Statistics*

Professor Bhaven Sampat provided a dataset containing all patents that have been listed in the FDA *Orange Book* for all 938 drugs approved from 1988 to 2005, which he has used to study the ability of academic patents to improve access to medicines.[77] This dataset was merged with publicly available data from the National Bureau of Economic Research (NBER) on patent assignees, which codes assignees as corporations, individuals, universities, institutes, or governments, and which indicates whether they are U.S. or foreign entities.[78] This data was also merged with data about which drug patents have been extended under 35 U.S.C. § 156, which was obtained from the U.S. Patent and Trademark Office (USPTO) website.[79]

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76. Univs. Allied for Essential Meds., UAEM's Response to the Statement of Principles and Strategies 3 (2010), *available at* http://essentialmedicine.org/archive/uaems-reponse-sps.

77. *See* Sampat, *supra* note 49.

78. The files used were "assignee.dta" and "patassg.dta.zip." *Downloads*, NBER Pat. Data Project, https://sites.google.com/site/patentdataproject/Home/downloads (last visited Mar. 1, 2010).

79. *Patent Term Extensions*, U.S. Pat. & Trademark Off., http://www.uspto.gov/patents/resources/terms/156.jsp (last visited Mar. 1, 2010). Each patent may only be extended

Summary statistics for the resulting dataset can be found in Table 1 in the Appendix. Of the 938 drugs, 380 were new chemical entities (NCEs). An NCE is a new molecule rather than, for instance, a new formulation of a molecule that already has FDA approval. FDA regulations define an NCE as "a drug that contains no active moiety that has been approved by FDA in any other application submitted under [the Hatch-Waxman Act]."[80]

Table 1 also shows that 228 of the 938 drugs received priority FDA review. Priority review, which is distinct from "Accelerated Approval" and "Fast Track Review,"[81] is available for a drug when "no satisfactory alternative therapy exists" or if the drug is "a significant improvement compared to marketed products."[82] Priority review is not limited to NCEs: 72 of the drugs receiving priority review were not NCEs, and 224 of the NCEs did not receive priority review.

Extended patent protection under 35 U.S.C. § 156 covered 453 of the 938 drugs. As discussed in Part I.B, one patent term extension of up to five years is allowed on each "product" for its "first permitted commercial marketing or use."[83] The meaning of "drug product" has been disputed; the Federal Circuit has rejected the USPTO's "active moiety" interpretation—the same standard used for defining NCEs—in favor of a more specific "active ingredient" standard, thus allowing extensions on more drugs.[84] Although all NCEs should be eligible for a patent term extension if they meet the requirements, a 1994 study found that about one-third of NCE developers from 1984 to 1992 did not file for extensions.[85] In this Note's 1988 to 2005 sample, extended patents cover forty

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once, but drugs covered by a patent that had been extended as part of an earlier NDA were flagged as having an extended patent because they still received the benefit of this longer protection.

80. 21 C.F.R. § 314.108(a) (2009). "Active moiety" is defined as "the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt . . . or other noncovalent derivative . . . of the molecule, responsible for the physiological or pharmacological action of the drug substance." *Id.*

81. For a concise summary of the FDA review programs, see SUSAN THAUL, CONG. RESEARCH SERV., RS 22814, FDA FAST TRACK AND PRIORITY REVIEW PROGRAMS (2008), *available at* http://www.nationalaglawcenter.org/assets/crs/RS22814.pdf.

82. OFFICE OF NEW DRUGS, FDA, MAPP 6020.3, REVIEW CLASSIFICATION POLICY: PRIORITY (P) AND STANDARD (S) 2 (2007), *available at* http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/ManualofPoliciesProcedures/ucm082000.pdf.

83. *See supra* notes 41–43 and accompanying text.

84. *See* PhotoCure ASA v. Kappos, 603 F.3d 1372, 1376–77 (Fed. Cir. 2010). For a discussion of the difference between "active ingredient" and "active moiety" in this context, see Erica J. Pascal, *The Billion-Dollar Naming Game: How Ambiguities in Patent Term Extension Provisions Allow Companies To Add Billions of Dollars to the Bottom Line*, 24 BIOTECHNOLOGY L. REP. 547, 551–52 (2005).

85. Suzan Kucukarslan & Jacqueline Cole, *Patent Extension Under the Drug Price Competition and Patent Term Restoration Act of 1994*, 49 FOOD & DRUG L.J. 511, 522 (1994).

percent of NCEs.[86] Of the 453 drugs with extended patents, 269 were NCEs, and 127 received priority approval.

Being an NCE, receiving priority approval, and having an extended patent are all independent variables, and there are some drugs with all possible combinations of these variables. There are 329 drugs that had none of these properties; these drugs form the baseline for the regressions discussed in Part III.B.

FIGURE 1
NUMBER OF DRUGS APPROVED BY THE FDA FROM 1988–2005

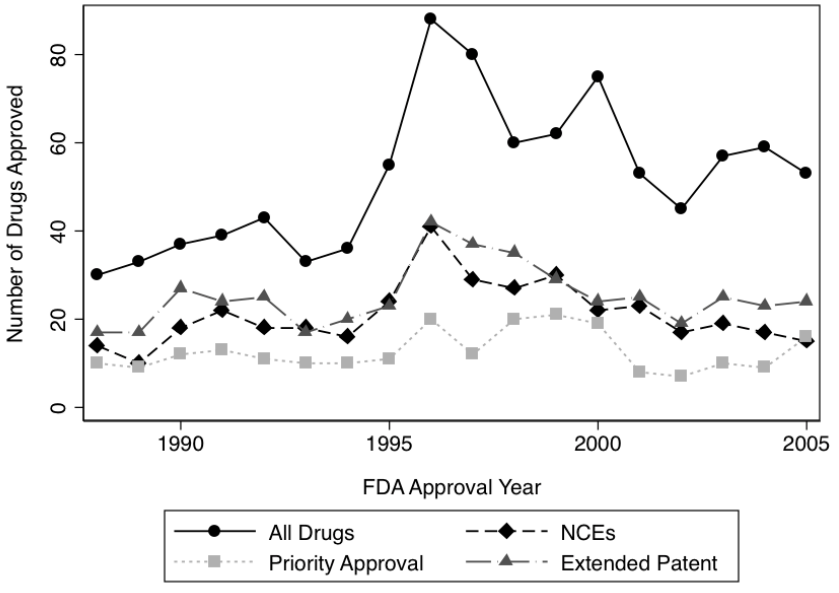

Figure 1 shows the number of FDA-approved drugs as a function of time from 1988 through 2005. It also separately shows the number of NCEs, drugs receiving priority approval, and drugs covered by extended patents.

There was a peak of eighty-eight drugs in 1996. The cause of the 1996 peak—and subsequent decline—is disputed. Some have hypothesized that the peak resulted from accelerated drug approval under the Prescription Drug User Fee Act of 1992 (PDUFA),[87] but that this was

86. Note that this is higher than the percent of NCEs that received a patent term extension, since multiple drugs can receive the benefit of one extended patent.

87. Pub. L. No. 102-571, 106 Stat. 4491 (codified as amended in scattered sections of 21 U.S.C.).

"not a stable state for either the industry or the FDA."[88] An empirical examination of this hypothesis, however, concluded that the peak was not due to PDUFA but that "[m]ore research is needed" to understand its cause.[89]

Professor Sampat's dataset also classified drugs by therapeutic class, such as anti-infective agents or cardiovascular agents. There are fifteen classes with more than three drugs in them, which were used as separate controls for some of the regressions. These classes are listed in Table 1. As the following section illustrates, different therapeutic groups often have different numbers of patents.

The bottom of Table 1 shows that these 938 drugs have had 1946 unique patents listed in the *Orange Book*, some of which are listed for multiple drugs. The vast majority of these patents (1824) have only private-sector assignees (corporations or individuals); 108 patents have only public-sector assignees (universities, institutes, hospitals, or governments). There are also fourteen patents with mixed public- and private-sector ownership. For example, one of the patents on the cancer drug Gleevec is jointly assigned to the pharmaceutical company Novartis, the Dana-Farber Cancer Institute, and Oregon Health and Science University.[90]

The following sections present some statistics, figures, and regressions based on this dataset to help answer the question of how many patents are used to protect the intellectual property for different types of drugs.

B. *Results: How Many Patents Does It Take To Make a Drug?*

Figure 2 shows the number of drugs that have had different numbers of patents listed in the *Orange Book*. Three hundred five drugs have had just one patent, while one drug—Evista, NDA number 20815—has had twenty-two patents listed. The average number of patents per drug is 2.97; the median number is two. Sixty-seven percent of drugs have more than one patent. These numbers show that the one-patent, one-drug assumption is generally inaccurate.[91]

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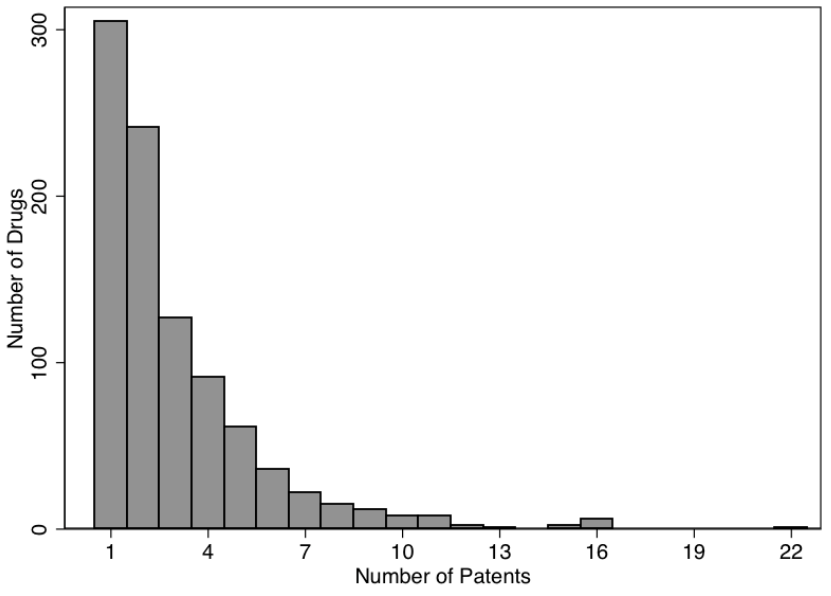
88. *E.g.*, Janice M. Reichert, *Trends in Development and Approval Times for New Therapeutics in the United States*, 2 NATURE REVS. DRUG DISCOVERY 695, 701 (2003).

89. James B. Graham, Trends in U.S. Regulatory Approvals of Biopharmaceutical Therapeutic Entities 63 (Apr. 5, 2005) (unpublished M.S. thesis, Massachusetts Institute of Technology), *available at* http://dspace.mit.edu/bitstream/handle/1721.1/30276/60847766.pdf.

90. U.S. Patent No. 6,958,335 (filed Oct. 26, 2001).

91. *See supra* notes 3–4 and accompanying text.

FIGURE 2
NUMBER OF DRUGS AS A FUNCTION OF PATENTS
LISTED IN THE FDA *ORANGE BOOK*



The average number of patents for different types of drugs is listed in the second column of Table 1. NCEs have slightly fewer patents than average (2.88), while drugs with priority approval or extended patents have more (3.41 and 3.10, respectively). The first column of Table 2 shows the coefficients from a regression in which the total number of patents on a drug is explained based on these three variables; the coefficients are statistically significant at the five or one percent level.[92]

The lower number of patents on NCEs may reflect the fact that these drugs can often be protected by simply having a single patent on the new molecule, whereas companies may actively seek additional patents on new formulations or on the use of an old molecule for a new indication. For example, the original NDA for the antiretroviral Zerit[93] had just one patent assigned to Yale University,[94] but the new formulation

92. The significance level indicates the likelihood that the effect was observed as a matter of chance if the null hypothesis is true. For an overview of statistical significance and other basic statistical tools that was written for federal judges, see David H. Kaye & David A. Freedman, *Reference Guide on Statistics*, *in* FED. JUDICIAL CTR., REFERENCE MANUAL ON SCIENTIFIC EVIDENCE 83 (2d ed. 2000).

93. NDA 20412 was approved in 1994. ORANGE BOOK, *supra* note 29 (search by application number for "20412").

94. U.S. Patent No. 4,978,655 (filed Dec. 17, 1986).

Zerit XR[95] listed both Yale's patent and a patent for a slow release of the original molecule, which was assigned to Bristol-Myers Squibb.[96] Similarly, the original NDA[97] for the schizophrenia drug Abilify listed just one patent for the new molecule,[98] while the new formulation of Abilify, approved two years later,[99] listed the original patent plus one for an oral solution of that molecule.[100]

The higher number of patents on drugs with priority approval or extended patents may reflect the increased importance of these drugs to pharmaceutical companies. If pharmaceutical companies predict higher sales for a drug or are more concerned about generic competitors, they may pursue a more aggressive patenting strategy. For example, the fifteen best-selling drugs from 2002 to 2004 have an average of over five patents per drug, higher than any of the individual categories in Table 1.[101]

The number of patents for a given drug has also been increasing over time, as noticed by Professors Hemphill and Sampat.[102] Figure 3 shows the average number of patents in the *Orange Book* as a function of the year a drug was approved by the FDA. The number of patents per drug is seen to increase from around 2.5 in the late 1980s to nearly 3.5 by 2005. The straight line shows a linear fit to the data. The second column of Table 2 shows that this increase over time is statistically significant.[103] This increase may be caused by increasingly aggressive patenting strategies, such as evergreening, by the pharmaceutical companies.[104] The

95. NDA 21453 was approved in 2002. ORANGE BOOK, *supra* note 29 (search by application number for "21453").

96. U.S. Patent No. 7,135,465 (filed Mar. 29, 2001).

97. NDA 21436 was approved in 2002. ORANGE BOOK, *supra* note 29 (search by application number for "21436").

98. U.S. Patent No. 5,006,528 (filed Oct. 20, 1989).

99. NDA 21713 was approved in 2004. ORANGE BOOK, *supra* note 29 (search by application number for "21713").

100. U.S. Patent No. 6,977,257 (filed Apr. 24, 2002).

101. The best-selling pharmaceutical products from 2002 to 2004 (with number of patents in parentheses) were Lipitor (five), Zocor (one), Plavix (five), Advair (five), Norvasc (two), Zyprexa (four), Paxil (seven), Nexium (thirteen), Zoloft (five), Celebrex (four), Effexor (one), Prevacid (eight), Diovan (three), Fosamax (eleven), and Risperdal (three). *See* Krishan Maggon, Editorial, *Best-Selling Human Medicines 2002–2004*, 10 DRUG DISCOVERY TODAY 739, 740 (2005). Also note that five patents per drug is lower than the "astounding 10 patents per drug" claimed by the President of the Generic Pharmaceutical Association. *Generic Pharmaceuticals: Marketplace Access and Consumer Issues: Hearing Before the S. Comm. on Commerce, Sci., & Transp.*, 107th Cong. 58 (2002) (statement of Kathleen Jaeger, President and CEO, Generic Pharmaceutical Association).

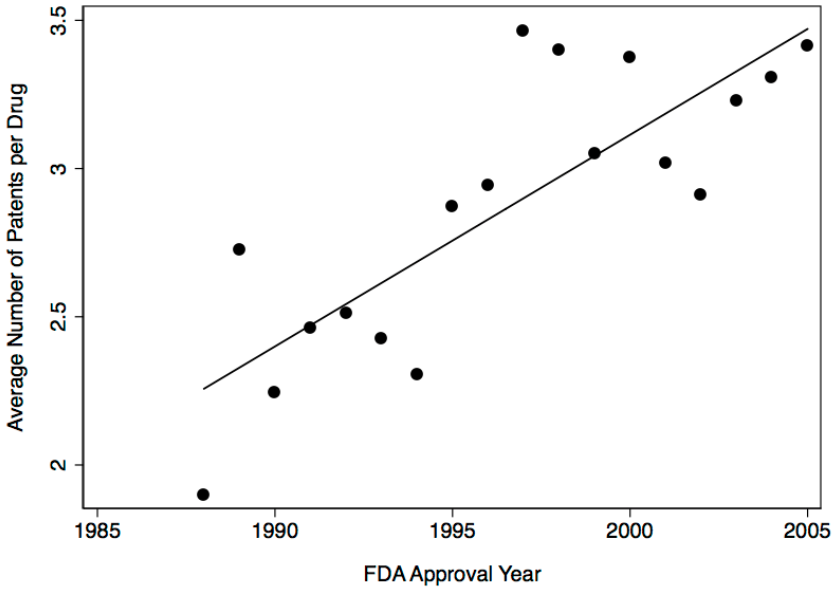
102. Hemphill & Sampat, *supra* note 6, at 1.

103. The coefficients in Table 2 are based on a negative binomial regression rather than a linear fit because the dependent variable is a nonnegative count variable.

104. *See supra* note 31 and accompanying text.

increase may also reflect changing standards for the granting of patents at the USPTO.[105]

FIGURE 3
AVERAGE NUMBER OF PATENTS LISTED IN THE FDA *ORANGE BOOK* AS A FUNCTION OF FDA APPROVAL YEAR WITH LINEAR FIT



The average number of patents also varies across therapeutic class. As seen in Table 1, the classes with the most patents are antihistamines (4.13) and antineoplastic agents (4.23),[106] while the classes with the fewest patents are drugs for electrolytic, caloric, and water balance (2.20) and skin and mucous membrane agents (1.79).[107] The fourth column of Table 2 controls for therapeutic class; this does not significantly affect the coefficients discussed above.

105. *Cf.* ADAM B. JAFFE & JOSH LERNER, INNOVATION AND ITS DISCONTENTS: HOW OUR BROKEN PATENT SYSTEM IS ENDANGERING INNOVATION AND PROGRESS, AND WHAT TO DO ABOUT IT 11 (2004) (arguing that the redesign of the USPTO in the early 1990s led to "a widely perceived decline in the rigor with which the standards of novelty and non-obviousness are applied in reviewing patent applications").

106. Antineoplastic agents are cancer drugs, such as Gleevec.

107. An F-test on the joint significance of therapy classes has a chi-squared p-value of 0.0004.

C. *Results: Public-Sector Patent Holders and Follow-On Patents*

As discussed in Part II, universities and other public-sector institutions hold many drug patents. The existence of follow-on patents on a drug has important implications for the socially responsible licensing goals of many of these institutions.

The bottom half of Table 1 shows the breakdown of patents by type of assignee. Of the 1946 unique patents in the dataset, 108 have only public-sector assignees. Another 14 of the 1946 patents have mixed private and public ownership, and private-sector assignees own the remainder. The 108 pure public-sector patents cover 77 different drugs; the 14 mixed-ownership patents cover 13. Two drugs have both a pure public-sector patent and a mixed-ownership patent, so the total number of drugs with any public-sector patent assignee is 88.

These 88 drugs are given in Table 3, which lists the 34 drugs that have only public-sector assignees on all of their patents, and in Table 4, which lists the 54 drugs with mixed ownership either on the same patent or on different patents.[108] In addition to listing the identity of the public-sector assignees and the year of approval, these tables also indicate which drugs are NCEs or received priority approval, as well as which drugs received a patent term extension and whether the extension was given to a public- or private-sector patent. Some of these drugs will be discussed in more detail in Part IV.

Table 5 examines the impact of public-sector patents on the number of patents on a drug. The first two columns show that having a public-sector assignee on at least one patent causes a very small and statistically insignificant increase in the total number of patents. However, when focusing only on whether there is more than one patent on a drug (rather than the total number of follow-on patents), the middle two columns show that there is a statistically significant increase in the likelihood of a follow-on patent when there is at least one public-sector assignee.

The relevant question for proponents of socially responsible licensing, however, is whether there is a *private-sector* follow-on patent. If there is simply a second public-sector patent, then that public-sector entity could follow the same access-promoting patenting strategy for both patents. The last two columns in Table 5 address this question and show that there is a decrease in the likelihood of a private-sector follow-on when there is a public-sector assignee. When controls for drug type and approval year are added, this decrease is statistically significant at the ten percent level.

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108. This list is similar to that given in Sampat, *supra* note 49, at 13 tbl.1.

Table 6 repeats the analyses of Table 5, but, in addition to looking at whether a drug has any public-sector patent assignees, it also separates the effects of mixed-ownership patents from those with only public-sector assignees. Having a pure public-sector patent has no statistically significant effect on the total number of patents on a drug, but it increases the likelihood of having at least one follow-on patent and decreases the likelihood of having a private-sector follow-on patent.[109] Having a mixed-ownership patent, on the other hand, is correlated with a statistically significant increase in the total number of patents, as well as a large increase in the likelihood of having a follow-on patent. The latter is only significant at the ten percent level, probably due to the small number of mixed-ownership patents.

Finally, Table 7 examines in more detail the impact of public-sector patents on whether there is a private follow-on patent. As seen the last column of Table 5, having a public-sector patent is correlated with a decreased likelihood of a private follow-on patent. This decrease becomes larger and more highly significant if we focus on public-sector patents that received a patent term extension (columns two and three) or public-sector patents that were the first-issued patent on a drug (columns five and six), which are those patents that are more likely to be the most important patents on a drug.

As a simpler way to think about this issue, without the additional controls of a regression: of the 850 drugs with no public-sector assignees, 562 (66%) have a follow-on patent. Of the 88 drugs with any public-sector assignees, 71 (81%) have a follow-on patent, but only 53 (60%) have a private-sector follow-on patent. In other words, university drugs are more likely to have follow-on patents than drugs without university patents. Because many of these follow-on patents are other public-sector patents, however, university drugs actually are less likely to have private-sector follow-on patents.

Even if university drugs are less likely to have a private-sector follow-on patent, over half of them still do. Organizations like UAEM are therefore right to worry that simply not filing public-sector patents in low- and middle-income countries will be insufficient to ensure generic access to public-sector drugs in those countries. The following Part looks in more detail at public-sector patent contributions to FDA-approved drugs.

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109. The increase is significant at the five percent level without controls; the decrease is significant at the ten percent level without controls and at the five percent level with controls.

IV. Case Studies in Public-Sector Pharmaceutical Patenting

As examined in Part III, drugs with patents from universities and other public-sector institutions are less likely to have additional private-sector patents than drugs with only private-sector patent assignees. Nonetheless, over half of public-sector drugs still have private-sector follow-on patents, which could act as a barrier to making these drugs accessible in low- and middle-income countries.

To examine this problem more closely, Table 8 lists detailed patent information for the eighteen drugs with both public- and private-sector patents that received FDA approval from 2001 through 2005, the most recent years in the dataset. This table lists all patents that have been published in the *Orange Book* for each drug; all assignees for those patents; the patents' filing, issue, and expiration years; and a brief description of the patent. For example, the first drug in Table 8, Alimta, is an NCE that received priority approval for treating lung cancer. Princeton University filed a patent on the drug molecule in 1991, which was granted in 1994.[110] Eli Lilly then filed a patent on using that molecule to treat tumors in 1992, which was granted in 1993.[111] Princeton licensed its patent to Eli Lilly in exchange for a percentage of net sales.[112] When Eli Lilly obtained FDA approval for Alimta, it extended Princeton's patent, which now expires in 2016. Eli Lilly was then issued an additional method-of-treatment patent in 2010, which expires in 2021.[113]

In addition to the assignees, two characteristics of the patenting patterns themselves are noteworthy. First, several of the drugs are not covered by any patent on the drug molecule itself. For example, although the Alzheimer's drug Namenda is an NCE, it is covered only by two method-of-treatment patents.[114] Similarly, the new formulation Zerit XR is covered by Yale's method-of-treatment patent and a patent on sustained-release beadlets owned by Bristol-Myers Squibb.[115] Second, many of the additional patents on these drugs are continuations, continuations-in-part, or divisions of earlier patents on the same drug. Since these "child" patents have the same expiration date as the parent, they will not have the effect of "evergreening" the drug's patent protection. For exam-

110. U.S. Patent No. 5,344,932 (filed Mar. 22, 1991).

111. U.S. Patent No. 5,217,974 (filed Sept. 4, 1992).

112. *See* Goldie Blumenstyk, *Princeton Claims Patent Infringement on a Blockbuster Lung-Cancer Drug*, Chron. Higher Educ. (May 6, 2009), http://chronicle.com/article/Princeton-Claims-Patent/42860.

113. U.S. Patent No. 7,772,209 (filed July 11, 2007).

114. U.S. Patent No. 5,614,560 (filed Apr. 11, 1995); U.S. Patent No. 5,061,703 (filed Apr. 11, 1990).

115. *See supra* notes 94 and 96 and accompanying text.

ple, as seen in Table 8, Velcade has eight patents listed in the *Orange Book*, but they stem from only two patent families.[116]

Turning to the patent assignees, it is noteworthy that public-sector patents were extended under 35 U.S.C. § 156 for six of the eighteen drugs in Table 8 and were the first-issued or first-filed patents for ten. In these situations, where the public-sector institution has an early or important patent, it is more likely to have stronger bargaining power to negotiate a proactive licensing agreement that ensures generic access in low- and middle-income countries. Conversely, for a drug like Gleevec, where the public-sector patent holders are joint patent owners with a pharmaceutical company, and where that patent was filed late in the FDA-approval process, those public-sector institutions probably have less bargaining power.[117]

Conclusion

This Note has presented the first extensive empirical analysis of follow-on drug patents. The number of patents per drug has increased over time, from around 2.5 in the late 1980s to nearly 3.5 by 2005. NCEs tend to have fewer patents, while drugs that received priority approval or that are covered by an extended patent tend to have more. Blockbuster drugs tend to have the highest numbers of patents, with an average of over five per drug from 2002 to 2004. These increasing numbers of patents may be related to relaxed patentability standards at the USPTO or to more aggressive patenting strategies on the part of pharmaceutical companies.

A more detailed look at drugs with patents owned by universities and other public-sector entities revealed that while university drugs tend to have more patents, they actually have fewer private-sector follow-on patents, especially when the university patent received a patent term extension or was the first-issued patent on a drug. Still, sixty percent of public-sector drugs do have private-sector patents. Therefore, policies focused on increasing access to university medicines by simply not patenting in low- and middle-income countries may be insufficient to ensure generic access to these drugs. Instead, public-sector institutions will need proactive licensing terms to ensure that follow-on patents do not block access to the end products that are needed by patients.

The number of universities and other public-sector institutions that follow socially responsible licensing practices is small but growing, and a number of universities recently committed to implementing and measuring the success of more specific strategies under the *Statement of*

116. Orange Book, *supra* note 29 (search by application number for "21602").
117. *See supra* note 90 and accompanying text.

Principles and Strategies.[118] Other universities should join this effort or adopt their own socially responsible licensing policies, both to further the goals of the Bayh-Dole Act and to promote global health through their role as public-spirited, knowledge-promoting institutions.

The results in this Note, however, indicate that some of the strategies in the *Statement of Principles and Strategies* may be insufficient to prevent patents from blocking access to medicines and other health-related technologies in developing countries. In particular, it seems unlikely that universities could ever "fully preclude intellectual property barriers to generic provision by not patenting in developing countries, or by filing and abandoning patents,"[119] because even if the public-sector patents are not a barrier, private-sector follow-on patents could be. Universities and other public-sector institutions should instead focus on other strategies from the *Statement of Principles and Strategies* that would prevent their private-sector partners from using follow-on patents to block access, such as "[r]eserved or 'march-in' rights, mandatory sublicenses or non-assert provisions."[120] Universities that develop their own socially responsible licensing policies, as well as those that choose to join and help revise the *Statement of Principles and Strategies*,[121] should emphasize the benefits of these and other proactive licensing strategies in promoting access to their inventions.

118. *See supra* note 74 and accompanying text.

119. Ass'n of Univ. Tech. Managers et al., *supra* note 74, at 2.

120. *Id.* at 3.

121. Signatories have committed to "[r]evisit these principles on a biennial basis," and the next revision should be released in the fall of 2011. *Id.* at 4. Discussions about these revisions are therefore likely to begin soon.

Appendix

Table 1
Descriptive Summary of Drug and Patent Data

FDA-Approved Drugs (1988–2005)	Number	Avg. Patents (Std. Dev.)
All drugs	**938**	**2.97 (2.55)**
New Chemical Entities (NCEs)	380	2.88 (2.41)
Priority approval	228	3.41 (2.87)
Received patent term extension	453	3.10 (2.62)
Therapeutic class		
Antihistamines	16	4.13 (2.96)
Anti-infective agents	123	3.45 (2.45)
Antineoplastic agents	57	4.23 (4.21)
Autonomic drugs	58	2.91 (2.42)
Blood formation and coagulation	13	2.92 (2.69)
Cardiovascular agents	100	2.89 (2.41)
Central nervous system agents	125	2.72 (2.32)
Diagnostic agents	31	2.84 (2.28)
Electrolytic, caloric, and water balance	10	2.20 (1.32)
Eye, ear, nose, and throat	50	2.62 (1.86)
Gastrointestinal drugs	55	3.11 (2.69)
Hormones and synthetic substitutes	93	3.10 (2.92)
Skin and mucous membrane agents	71	1.79 (1.34)
Smooth muscle relaxants	6	4.00 (3.79)
Vitamins	6	3.83 (2.48)
Other classes	124	2.80 (2.15)
Patent ownership		
Only public-sector assignees on all patents	34	2.03 (1.34)
Mixed public/private ownership	54	3.96 (2.48)
Only private-sector assignees on all patents	850	2.95 (2.58)
Patents in *Orange Book*	**Number**	**Number of Drugs**
All patents (counting twice if on two drugs)	2788	938
Unique patents (counting once if on two drugs)	1946	938
Only private-sector assignees	1824	902
Only public-sector assignees	108	77
U.S. universities	52	39
U.S. institutes	25	16
U.S. government	15	15
Foreign public-sector	16	8
Mixed public/private sector on same patent	14	13

Notes: "Number of Drugs" at bottom right refers to drugs with at least one patent of that type, not drugs with only patents of that type.

TABLE 2
NUMBER OF PATENTS ON FDA-APPROVED DRUGS (1988–2005)

	Dependent Variable: Number of Patents			
	(1)	**(2)**	**(3)**	**(4)**
NCE	-0.170*** (0.063)		-0.156** (0.063)	-0.156** (0.063)
Priority approval	0.238*** (0.065)		0.250*** (0.065)	0.209*** (0.070)
Extended patent	0.121** (0.062)		0.140** (0.062)	0.121** (0.060)
Approval year		0.024*** (0.006)	0.025*** (0.006)	0.023*** (0.006)
Therapeutic class fixed effects	No	No	No	Yes

Notes: The dependent variable in each negative binomial regression is the number of patents that have been listed in the FDA's *Orange Book* for each drug.

Independent variables (listed in separate rows) are (1) whether the drug is a new chemical entity (NCE), (2) whether the drug received priority FDA approval, (3) whether any of the drug's patents were extended under 35 U.S.C. § 156, (4) the FDA approval year for the drug, and (5) controls for the therapeutic class of the drug.

Robust standard errors are in parentheses. Asterisks indicate statistical significance at the ***1%, **5%, and *10% levels. N = 938 for all columns.

Table 3
Drugs with Only Public-Sector Patent Assignees

NDA	Tradename	Year	Patents	Patent Assignee(s)
20162	Acthrel[np]	1996	1	Salk Institute
20747	Actiq	1998	2	University of Utah
19937	Adenocard[np]	1989	1	University of Virginia
20404	Avita	1997	2	University of California
20954	Busulfex[p]	1999	2	University of Houston; University of Texas
21673	Clolar[np]	2004	2[e]	Southern Research Institute
18511	DTPA	1989	1	U.S. Government, DOE
20193	Elmiron[n]	1996	1	University of California
21500	Emtriva[n]	2003	5[e]	Emory University
21896	Emtriva[p]	2005	5[e]	Emory University
19677	Enlon-Plus	1991	1	University of California
20044	Exosurf Neonatal[np]	1990	3[e]	University of California
20038	Fludara[np]	1991	1[e]	U.S. Government, HHS
19863	Geref[n]	1990	2[e]	Salk Institute
20443	Geref	1997	2[e]	Salk Institute
20845	Inomax[np]	1999	2	Mass. General Hospital
20388	Navelbine[np]	1994	1[e]	French Government
21544	Seasonale	2003	1	Medical College of Hampton Roads
21084	SERPACWA[np]	2000	1	U.S. Government, Army
19890	Stadol	1991	1	University of Kentucky
19836	Supprelin[np]	1991	1[e]	Salk Institute
20898	Thyrogen[np]	1998	2	Sloan-Kettering
21248	Trisenox[np]	2000	4	Sloan-Kettering
19981	Ultratag	1991	1	Associated Universities
20155	Videx[p]	1991	3	U.S. Government, HHS
20156	Videx[p]	1991	3	U.S. Government, HHS
21183	Videx EC[p]	2000	2	U.S. Government, HHS
20638	Vistide[n]	1996	1[e]	Czech Academy of Sciences
20569	Vitrasert[p]	1996	1	University of Kentucky
21636	Zegerid	2004	5	University of Missouri
21706	Zegerid	2004	5	University of Missouri
21606	Zemplar	2005	2[e]	University of Wisconsin
20412	Zerit[np]	1994	1[e]	Yale University
20413	Zerit[p]	1996	1[e]	Yale University

Notes: List of all thirty-four drugs approved 1988–2005 with only public-sector patent assignees. NDA = new drug application number; [n] = new chemical entity (NCE); [p] = priority approval; Year = FDA approval year; Patents = number of patents in *Orange Book*; [e] = patent extended under 35 U.S.C. § 156 (not necessarily as part of this NDA); HHS = Department of Health and Human Services; DOE = Department of Energy.

Table 4
Drugs with Public- and Private-Sector Patents

NDA	Tradename	Year	Patents	Public-Sector Assignee(s)
21462	Alimta[np]	2004	2 (1[e])	Princeton University
20625	Allegra[n]	1996	12[e] (1)	Georgetown University
20786	Allegra-D 12 Hour	1997	11[e] (1)	Georgetown University
21316	Altoprev	2002	3 (1)	Children's Hospital Boston
19785	Cardiolite[n]	1990	5 (1[ei])	Massachusetts Institute of Technology; Harvard College
21392	Cardizem LA	2003	4 (1)	University of Gent
19829	Ceretec[np]	1988	2 (1[i])	University of Missouri
21197	Cetrotide[n]	2000	4 (1[e])	Tulane University
21835	Clobex	2005	2 (1)	University of Tennessee
20869	Cosopt	1998	4[e] (1[i])	University of Florida
21283	Diovan	2001	3 (1)	Brigham & Women's Hospital
20221	Ethyol[np]	1995	4 (1)	University of Arizona
20989	Evoxac[n]	2000	2 (1[ei])	Israeli Government
20195	Fentanyl[p]	1993	2 (1[i])	University of Utah
21481	Fuzeon[np]	2003	3 (2[ei])	Duke University
21335	Gleevec[np]	2001	3[e] (1)	Oregon Health & Science University; Dana Farber Cancer Institute
21588	Gleevec	2003	3[e] (1)	Oregon Health & Science University; Dana Farber Cancer Institute
20637	Gliadel[p]	1996	3 (2[i])	Massachusetts Institute of Technology
20076	Habitrol	1991	3 (2)	University of California
21449	Hepsera[np]	2002	2 (1[i])	Czech Academy of Sciences
20199	Hivid[np]	1992	2 (1[i])	U.S. Government, HHS
20965	Levulan[n]	1999	5 (4[ei])	Queens University of Kingston
21446	Lyrica[np]	2004	3 (2[ei])	Northwestern University
21674	Menostar	2004	3 (2)	University of California; Kaiser Foundation
20586	Meretek UBT Kit[n]	1996	2[e] (1)	Balyor College of Medicine
20098	Mivacron[np]	1992	1[e] (1[i])	Mass. General Hospital
21487	Namenda[n]	2003	2 (1)	Children's Hospital Boston
20326	Neutrexin[np]	1993	3[e] (1)	U.S. Government, HHS
19927	Nizoral	1990	2 (1)	University of Tennessee
20310	Nizoral A-D	1997	2 (1[i])	University of Tennessee
20886	Panretin[np]	1999	2 (2[i])	Balyor College of Medicine; Salk Institute
20958	Pepcid Complete	2000	3 (1[i])	Brigham & Women's Hospital
21320	Plenaxis[np]	2003	6 (3[ei])	Indiana University
21688	Sensipar[np]	2004	4 (2[i])	Brigham & Women's Hospital
19608	Sildaflo	1989	2 (1[i])	Research Corporation
21106	Somavert[np]	2003	6[e] (4[i])	Ohio University
20657	Sporanox[p]	1997	5[e] (1)	U.S. Government, HHS
21055	Targretin[np]	1999	5 (1[i])	La Jolla Cancer Research Foundation
20262	Taxol[np]	1992	3 (1[i])	U.S. Government, HHS

NDA	Tradename	Year	Patents	Public-Sector Assignee(s)
20785	Thalomid[np]	1998	10 (2[f])	Children's Hospital Boston
19979	Ticlid[np]	1991	2 (1[ef])	French Government
20505	Topamax[n]	1996	4[e] (3)	New England Medical Center
20844	Topamax Sprinkle	1998	5[e] (3)	New England Medical Center
20408	Trusopt[np]	1994	2[e] (1[f])	University of Florida
21752	Truvada[p]	2004	9 (5[ef])	Emory University
21602	Velcade[np]	2003	6[e] (2)	U.S. Government, HHS
21267	Vfend	2002	7[e] (2)	University of Kansas
20154	Videx[np]	1991	4 (3[f])	U.S. Government, HHS
21119	Visudyne[np]	2000	10 (7[ef])	Massachusetts General Hospital; University of British Columbia
20961	Vitravene[np]	1998	4 (2[f])	U.S. Government, HHS
20597	Xalatan[np]	1996	5 (1[ef])	Columbia University
20819	Zemplar[n]	1998	4 (2[ef])	University of Wisconsin
21453	Zerit XR	2002	2 (1[ef])	Yale University
20212	Zinecard[np]	1995	2 (1)	New York University

Notes: Table lists all fifty-four drugs approved 1988–2005 with both private- and public-sector patent assignees among all listed patents. NDA = new drug application number; [n] = new chemical entity (NCE); [p] = priority approval; Year = FDA approval year; Patents = total number of patents in *Orange Book* (with number of public-sector patents in parentheses); [e] = patent covering drug was extended under 35 U.S.C. § 156 (outside parentheses = private-sector patent; inside parentheses = public-sector patent); [f] = public-sector patent is first issued patent for this drug; HHS = Department of Health and Human Services; DOE = Department of Energy.

TABLE 5
IMPACT OF PUBLIC-SECTOR PATENTS ON FOLLOW-ON PATENTS

	Dependent Variable:					
	Number of Patents		**Follow-On (Dummy)**		**Private Follow-On (Dummy)**	
	(1)	**(2)**	**(3)**	**(4)**	**(5)**	**(6)**
Public-sector assignee	0.087 (0.082)	0.009 (0.085)	0.761*** (0.280)	0.612** (0.300)	-0.254 (0.230)	-0.461* (0.259)
NCE		-0.157** (0.063)		-0.326* (0.175)		-0.235 (0.172)
Priority approval		0.208*** (0.072)		0.584*** (0.211)		0.519** (0.204)
Extended patent		0.121** (0.060)		0.357** (0.163)		0.329** (0.159)
Approval year		0.023*** (0.006)		0.059*** (0.016)		0.051*** (0.016)
Therapeutic class fixed effects	No	Yes	No	Yes	No	Yes

Notes: The dependent variable for the negative binomial regressions in the first two columns is the number of patents that have been listed in the FDA's *Orange Book* for each drug. The dependent variables for the logistic regressions in the last four columns are dummy variables for whether the drug has more than one patent in the *Orange Book*; for the last two columns, at least one of these patents must be a private-sector patent.

Independent variables (listed in separate rows) are (1) whether the drug has any public-sector patent assignee, (2) whether the drug is a new chemical entity (NCE), (3) whether the drug received priority FDA approval, (4) whether any of the drug's patents were extended under 35 U.S.C. § 156, (5) the FDA approval year for the drug, and (6) controls for the therapeutic class of the drug.

Robust standard errors are in parentheses. Asterisks indicate statistical significance at the ***1%, **5%, and *10% levels. N = 938 for all columns.

Table 6
Impact of Pure Public-Sector or Mixed Patents on Follow-On Patents

	Dependent Variable:					
	Number of Patents		Follow-On (Dummy)		Private Follow-On (Dummy)	
	(1)	(2)	(3)	(4)	(5)	(6)
Pure public-sector patent	0.008 (0.078)	-0.077 (0.081)	0.644** (0.291)	0.475 (0.312)	-0.468* (0.242)	-0.706** (0.276)
Public/private mixed patent	0.497** (0.204)	0.485** (0.216)	1.738* (1.042)	1.753 (1.098)	1.903* (1.056)	1.918* (1.105)
NCE		-0.163*** (0.062)		-0.333* (0.175)		-0.251 (0.172)
Priority approval		0.200*** (0.072)		0.564*** (0.211)		0.482** (0.205)
Extended patent		0.120** (0.060)		0.357** (0.163)		0.330** (0.160)
Approval year		0.023*** (0.006)		0.057*** (0.016)		0.047*** (0.016)
Therapeutic class fixed effects	No	Yes	No	Yes	No	Yes

Notes: The dependent variable for the negative binomial regressions in the first two columns is the number of patents that have been listed in the FDA's *Orange Book* for each drug. The dependent variables for the logistic regressions in the last four columns are dummy variables for whether the drug has more than one patent in the *Orange Book*; for the last two columns, at least one of these patents must be a private-sector patent.

Independent variables (listed in separate rows) are (1) whether the drug has a patent assigned to only private-sector entities, (2) whether the drug has a mixed-ownership patent (assigned to both public- and private-sector entities), (3) whether the drug is a new chemical entity (NCE), (4) whether the drug received priority FDA approval, (5) whether any of the drug's patents were extended under 35 U.S.C. § 156, (6) the FDA approval year for the drug, and (7) controls for the therapeutic class of the drug.

Robust standard errors are in parentheses. Asterisks indicate statistical significance at the ***1%, **5%, and *10% levels. N = 938 for all columns.

TABLE 7
IMPACT OF IMPORTANT PUBLIC-SECTOR PATENTS ON PRIVATE FOLLOW-ON PATENTS

	Dependent Variable: Private Follow-On (Dummy)				
	(1)	(2)	(3)	(4)	(5)
Public-sector patent	-0.461* (0.259)				
Public-sector patent extended		-0.665* (0.385)	-1.179** (0.475)		
Public-sector patent issued first				-0.863*** (0.259)	-1.161*** (0.312)
NCE	-0.235 (0.172)		-0.232 (0.172)		-0.216 (0.173)
Priority approval	0.519** (0.204)		0.511** (0.204)		0.633*** (0.212)
Extended patent	0.329** (0.159)		0.416*** (0.160)		0.305* (0.160)
Approval year	0.051*** (0.016)		0.053*** (0.016)		0.050*** (0.016)
Therapeutic class fixed effects	Yes	No	Yes	No	Yes

Notes: The dependent variable for each logistic regression is a dummy variable for whether the drug has more than one patent in the *Orange Book* with at least one private-sector patent.

Independent variables (listed in separate rows) are (1) whether the drug has any public-sector patent assignee, (2) whether the drug received a patent term extension on a public-sector patent, (3) whether the drug's first issued patent was a public-sector patent, (4) whether the drug is a new chemical entity (NCE), (5) whether the drug received priority FDA approval, (6) whether any of the drug's patents were extended under 35 U.S.C. § 156, (7) the FDA approval year for the drug, and (8) controls for the therapeutic class of the drug.

The first column is identical to the last column in Table 5, and is included for ease of comparison.

Robust standard errors are in parentheses. Asterisks indicate statistical significance at the ***1%, **5%, and *10% levels. N = 938 for all columns.

Table 8
Detailed Patent Information for the 18 Drugs with Public- and Private- Sector Patents That Received FDA Approval from 2001–05

Alimta (Pemetrexed Disodium)—NCE, Priority Approval

NDA	**FDA Applicant**	**Approval**	**Indication (Therap. Grp.)**
21462	Eli Lilly	2004	lung cancer (antineoplastic)
Patent	**Assignee**	**File/Issue/Exp.**	**Description**
5217974	Eli Lilly	1992/1993/2011	method of treatment
5344932[e]	Princeton Univ.	1991/1994/2016	NCE
7772209[n]	Eli Lilly	2007/2010/2021	method of treatment

Altoprev (lovastatin)—new formulation

NDA	**FDA Applicant**	**Approval**	**Indication (Therap. Grp.)**
21316	Andrx Labs.	2002	cholesterol (cardiovascular)
Patent	**Patent Assignee**	**File/Issue/Exp.**	**Description**
5916595	Andrx Pharms.	1997/1999/2017	controlled-release formulation
6080778	Children's Hosp. Boston	1998/2000/2018	method of treatment
6485748	Andrx Pharms.	1997/2002/2017	controlled-release formulation (continuation of '595)

Cardizem LA (diltiazem hydrochloride)—new formulation

NDA	**FDA Applicant**	**Approval**	**Indication (Therap. Grp.)**
21392	Biovail Labs. Int'l	2003	hypertension (cardiovascular)
Patent	**Assignee**	**File/Issue/Exp.**	**Description**
5288505	Galephar P.R.	1991/1994/2011	extended-release formulation
5529791	Galephar P.R.	1994/1996/2013	extended-release formulation (continuation of '505)
6923984	Univ. of Gent	2000/2005/2021	wax beads for holding biologically active ingredients
7108866	Biovall Labs. Int'l	2000/2005/2019	controlled-release formulation; method of treatment

Clobex (clobetasol)—new formulation

NDA	**FDA Applicant**	**Approval**	**Indication (Therap. Grp.)**
21835	Galderma Labs	2005	psoriasis (skin & mucus membrane)
Patent	**Assignee**	**File/Issue/Exp.**	**Description**
5972920	Dermalogix Partners	1998/1999/2018	new formulation
5990100	Univ. of Tenn.; Panda Pharms.	1998/1999/2018	composition; method of treatment

Diovan (valsartan)—new formulation

NDA	**FDA Applicant**	**Approval**	**Indication (Therap. Grp.)**
21283	Novartis	2001	hypertension (cardiovascular)
Patent	**Assignee**	**File/Issue/Exp.**	**Description**
5399578	Ciba-Geigy	1992/1995/2012	NCE; method of treatment
5972990	Brigham & Women's Hosp.	1992/1999/2016	method of treatment
6294197	Novartis	1999/2001/2017	oral dosage form

Fuzeon (enfuvirtide)—NCE, priority approval

NDA	**FDA Applicant**	**Approval**	**Indication (Therap. Grp.)**
21481	Roche	2003	HIV (anti-infective)
Patent	**Assignee**	**File/Issue/Exp.**	**Description**
5464933	Duke Univ.	1993/1995/2013	NCE
6133418[e]	Duke Univ.	1995/2000/2014	NCE (child of '933)
6475491	Trimeris	1998/2002/2015	method of treatment; composition

Gleevec (imatinib mesylate)—NCE (priority approval) and new formulation

NDA	**FDA Applicant**	**Approval**	**Indication (Therap. Grp.)**
21335	Novartis	2001	cancer (antineoplastic)
21588	Novartis	2003	cancer (antineoplastic)
Patent	**Assignee**	**File/Issue/Exp.**	**Description**
5521184[e]	Ciba-Geigy	1994/1996/2015	NCE; method of treatment
6894051	Novartis	1998/2005/2019	crystalline form; method of treatment
6958335	Oregon Health & Sci. Univ.; Dana-Farber Cancer Inst.; Novartis	2001/2005/2021	method of treatment
7544799[n]	Novartis	2006/2009/2019	crystalline form (child of '051)

Hepsera (adefovir dipivoxil)—NCE, priority approval

NDA	**FDA Applicant**	**Approval**	**Indication (Therap. Grp.)**
21449	Gilead	2002	hepatitis B (anti-infective)
Patent	**Assignee**	**File/Issue/Exp.**	**Description**
5663159	Czech Acad. of Scis.; Rega Stichting v.z.w.	1994/1997/2014	NCE; method of treatment
6451340	Gilead	2001/2002/2018	crystalline form; method of treatment

Lyrica (pregabalin)—NCE, priority approval

NDA	**FDA Applicant**	**Approval**	**Indication (Therap. Grp.)**
21446	CP Pharms.	2004	nerve pain (central nervous system)
Patent	**Assignee**	**File/Issue/Exp.**	**Description**
5563175	Northwestern Univ.; Warner-Lambert	1995/1996/2013	method of treatment
6001876[e*]	Warner-Lambert	1998/1999/2018	method of treatment
6197819[e]	Northwestern Univ.	1995/2001/2018	NCE (same family as '175)
*The '876 patent was extended under Lyrica NDA No. 21723.			

Menostar (estradiol)—new indication

NDA	**FDA Applicant**	**Approval**	**Indication (Therap. Grp.)**
21674	Bayer	2004	osteoporosis prevention (hormones & synthetic substitutes)
Patent	**Assignee**	**File/Issue/Exp.**	**Description**
5223261	Riker Labs.	1991/1993/2010	patch for delivering drug through skin; method of treatment
5891868	Univ. of Cal.; Kaiser Found.; Berlex Labs.; Permanente Med. Grp.	1997/1999/2017	method of treatment
6692763	Univ. of Cal.; Kaiser Found.; Berlex Labs.; Permanente Med. Grp.	2000/2004/2017	method of treatment (very similar claims to '868)

Namenda (memantine hydrochloride)—NCE

NDA	**FDA Applicant**	**Approval**	**Indication (Therap. Grp.)**
21487	Forest Labs	2003	Alzheimer's (central nervous system)
Patent	**Assignee**	**File/Issue/Exp.**	**Description**
5061703[e*]	Merz GmbH & Co.	1990/1991/2015	method of treatment
5614560[**]	Children's Hospital Boston	1995/1997/2014	method of treatment
*Extended after the data on patent term extensions was obtained from the USPTO website. **No longer listed in the *Orange Book*.			

Plenaxis (abarelix)—NCE, priority approval

NDA	**FDA Applicant**	**Approval**	**Indication (Therap. Grp.)**
21320	Speciality European	2003	prostate cancer (antineoplastic)
Patent	**Assignee**	**File/Issue/Exp.**	**Description**
5843901[e]	Advanced Research & Tech. Inst. (Indiana Univ.)	1995/1998/2015	NCE
5968895	Praecis Pharms.	1996/1999/2016	composition
6180608	Praecis Pharms.	1997/2001/2016	formulation; method of treatment (child of '895)
6423686	Advanced Research & Tech. Inst. (Indiana Univ.)	1998/2002/2015	NCE (child of '901)
6455499	Indiana Univ.	1999/2002/2015	method of treatment (child of '686)
6699833	Praecis Pharms.	1999/2004/2016	composition (child of '895)

Sensipar (cinacalcet hydrochloride)—NCE, priority approval

NDA	**FDA Applicant**	**Approval**	**Indication (Therap. Grp.)**
21688	Amgen	2004	secondary hyperparathyroidism, hypercalcaemia (other)
Patent	**Assignee**	**File/Issue/Exp.**	**Description**
6011068	Brigham & Women's Hosp.; NPS Pharms.	1994/2000/2016	NCE
6031003	Brigham & Women's Hosp.; NPS Pharms.	1995/2000/2016	method of treatment (child of '068)
6211244	NPS Pharms.	1995/2001/2015	NCE; method of treatment
6313146	NPS Pharms.	1995/2001/2016	NCE (child of '068)

Somavert (pegvisomant)—NCE, priority approval

NDA	**FDA Applicant**	**Approval**	**Indication (Therap. Grp.)**
21106	Pharmacia and Upjohn	2003	acromegaly (hormones & synthetic substitutes)
Patent	**Assignee**	**File/Issue/Exp.**	**Description**
5350836	Ohio Univ.	1992/1994/2011	NCE
5681809	Ohio Univ.	1994/1997/2011	NCE; method of treatment (child of '836)
5849535[e]	Genentech	1996/1998/2017	NCE; method of preparation
5958879	Ohio Univ.	1995/1999/2011	NCE; method of treatment (child of '809)
6057292	Genentech	1998/2000/2015	method of treatment (child of '535)
6583115	Ohio Univ.	1995/2003/2011	NCE; method of treatment (child of '809)

Truvada (emtricitabine; tenofovir disoproxil fumarate)—new comb., priority

NDA	**FDA Applicant**	**Approval**	**Indication (Therap. Grp.)**
21752	Gilead	2004	HIV (anti-infective)
Patent	**Assignee**	**File/Issue/Exp.**	**Description**
5210085	Emory Univ.	1991/1993/2010	method of treatment
5814639	Emory Univ.	1993/1998/2015	NCE (child of '085)
5914331[e*]	Emory Univ.	1995/1999/2017	NCE (child of '085)
5922695	Gilead	1997/1999/2017	NCE; method of treatment; method of preparation
5935946	Gilead	1997/1999/2017	NCE; method of treatment; method of preparation
5977089	Gilead	1998/1999/2017	NCE; method of treatment (child of '695)
6043230	Gilead	1999/2000/2017	method of preparation (child of '695)
6642245	Emory Univ.	1995/2003/2020	method of treatment (child of '085)
6703396	Emory Univ.	1995/2004/2021	NCE (child of '085)
7402588[n]	Emory Univ.	2006/2008/2010	method of treatment; composition (child of '085)
*Extended for the drug Emtriva (NDA 21500), one of the components in Truvada.			

Velcade (bortezomib)—NCE, priority approval

NDA	**FDA Applicant**	**Approval**	**Indication (Therap. Grp.)**
21602	Millennium Pharms.	2003	multiple myeloma, mantle cell lymphoma (antineoplastic)
Patent	**Assignee**	**File/Issue/Exp.**	**Description**
5780454[e]	ProScript	1995/1998/2017	NCE
6083903	LeukoSite	1995/2000/2014	NCE; method of treatment (same family as '454)
6297217	Millennium Pharms.	2000/2001/2014	method of treatment (division of '454)
6617317	Millennium Pharms.	2002/2003/2013	NCE (child of '217)
6713446	U.S. Gov't, HHS	2002/2004/2022	NCE; method of preparation
6747150[n]	Millennium Pharms.	2003/2004/2014	NCE (child of '317)
6958319	U.S. Gov't, HHS	2003/2005/2022	NCE; method of preparation (child of '446)
7119080[n]	Millennium Pharms.	2003/2006/2014	NCE (child of '317)

Vfend (voriconazole)—new formulation

NDA	**FDA Applicant**	**Approval**	**Indication (Therap. Grp.)**
21267	Pfizer	2002	fungal infections (anti-infective)
Patent	**Assignee**	**File/Issue/Exp.**	**Description**
5116844	Pfizer	1989/1992/2009	composition for treatment; method of treatment
5134127	Univ. of Kansas	1990/1992/2010	NCE
5364938	Pfizer	1993/1994/2011	NCE (child of '844)
5376645	Univ. of Kansas	1992/1994/2010	NCE (child of '127)
5567817[e]	Pfizer	1995/1996/2016	NCE; method of treatment
5773443	Pfizer	1996/1998/2011	NCE; method of treatment (child of '817)
6632803	Pfizer	1999/2003/2018	formulation

Zerit XR (stavudine)—new formulation

NDA	**FDA Applicant**	**Approval**	**Indication (Therap. Grp.)**
21453	Bristol-Myers Squibb	2002	HIV (anti-infective)
Patent	**Assignee**	**File/Issue/Exp.**	**Description**
4978655[e*]	Yale Univ.	1986/1990/2008	method of treatment
7135465	Bristol-Myers Squibb	2001/2006/2023	sustained release beadlets
*Extended for the drug Zerit (NDA 20412).			

Notes: Each sub-table gives the proprietary trade name of the FDA-approved drug (with the active ingredient in parentheses), the new drug application (NDA) number for the drug, the company that applied for FDA approval, the year of FDA approval, the conditions for which the drug is indicated (with the therapeutic group in parentheses). The second part of each sub-table lists all patents that have been listed in the *Orange Book* for that drug; all assignees for those patents; the filing, issue, and expiration years; and a brief description of the patent. The superscript [e] indicates that a patent was extended under 35 U.S.C. § 156 (though the extension may have been granted as part of an

earlier NDA, as for Zerit XR). The superscript [n] indicates that a patent was newly added to the *Orange Book* after the creation of the dataset used for the analyses in Tables 1 through 7. "Child" patents are continuations, divisions, or continuations-in-part; patents in the same "family" are children of the same patent.