Petrie-Flom Center for Health Law Policy, Biotechnology & Bioethics at Harvard Law School

DRAFT
Publication forthcoming in the *Texas Law Review*, Volume 87

Unpatentable Drugs and the Standards of Patentability

Benjamin N. Roin*

May 1, 2008

The role of the patent system in promoting pharmaceutical innovation is widely seen as a tremendous success story. This view overlooks a serious shortcoming in the drug patent system: the standards by which drugs are deemed unpatentable under the novelty and non-obviousness requirement bear little relationship to the social value of those drugs or the need for a patent to motivate their development. If the idea for a drug is not novel or is obvious, perhaps because it was disclosed in an earlier publication or made to look obvious by recent scientific advances, then it cannot be patented. Yet the mere idea for a drug alone is generally of little value to the public. Without clinical trials proving the drug's safety and efficacy, a prerequisite for FDA approval and acceptance by the medical community, it is unlikely to benefit the public. Given the immense investment needed to fund clinical trials on drugs, and the ability of generic manufacturers to rely on those tests to secure regulatory approval for their own products, pharmaceutical companies are rarely willing to develop a drug without patent protection. The novelty and non-obviousness requirements make no concession for the development costs of inventions, and thus withhold patents from drugs that are unlikely to reach the public without that protection. This gap in the patent system for drugs has created a pervasive problem in the pharmaceutical industry, causing firms to regularly screen through their drugs in R&D and discard ones with weak patent protection. The potential harm to the public from the loss of these drugs is likely significant. Congress can easily avoid this problem by ensuring that the successful completion of the FDA's rigorous clinical trial process is rewarded with a lengthy exclusivity period enforced by the FDA.

* Academic Fellow, Petrie-Flom Center for Health Law Policy, Biotechnology & Bioethics. I would like to thank Omri Ben-Shahar, Yochai Benkler, Eric Budish, Glenn Cohen, Arthur Daemmrich, Rochelle Dreyfuss, Rebecca Eisenberg, Terry Fisher, Paul Goldstein, Joseph Grundfest, Richard Hamermesh, Valerie Junod, Mark Lemley, Saul Levmore, Jessica Litman, Holly Lynch, Jonathan Masur, Judge Michael McConnell, David McGowan, Michael Meurer, Abby Moncrieff, Dotan Oliar, Kevin Outterson, Margaret Radin, Arti Rai, Howard Roin, Julie Roin, Pamela Samuelson, Kathryn Spier, Chris Sprigman, Mark Stein, Talha Syed, Lloyd Weinreb, and the participants at the Harvard Law and Economics workshop and the Petrie-Flom Center workshop. I am especially indebted to my wife, Gretchen, for her invaluable suggestions, and to Jennifer Arlen, Einer Elhauge, Louis Kaplow and Steven Shavell for their insightful comments.

UNPATENTABLE DRUGS AND THE STANDARDS OF PATENTABILITY

Benjamin N. Roin

INTRODUCTION

Pharmaceutical patents are often held out as an example of the patent system at its best.[1] It is widely accepted that patents play an essential role in motivating private investment in pharmaceutical R&D, and those investments have yielded tremendous social gains through the introduction of new medical treatments. For this reason, pharmaceutical innovation is thought to be the patent system's greatest success story.

Amidst this general optimism about the effectiveness of patents in promoting pharmaceutical innovation, scholars have overlooked a critical flaw in the system: socially valuable drugs often cannot be patented even though they are unlikely to be developed for public use without that protection. If the idea for a drug is not novel or is

[1] *See* JAMES BESSEN & MICHAEL J. MEURER, PATENT FAILURE: HOW JUDGES, BUREAUCRATS, AND LAWYERS PUT INNOVATION AT RISK 88-89 (2008); 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 39-41 (2004).

obvious, perhaps because it was disclosed in an earlier publication or made to look obvious by recent scientific advances, then it cannot be patented. Yet the mere idea for a drug alone is generally of little value to the public. Without clinical trials proving the drug's safety and efficacy, a prerequisite for Food and Drug Administration ("FDA") approval and acceptance by the medical community, it is unlikely to benefit the public. Given the immense investment needed to fund clinical trials on drugs, and the ability of generic manufacturers to rely on those tests to secure regulatory approval for their own products, pharmaceutical companies are rarely willing to develop a drug without patent protection. The novelty and non-obviousness requirements make no concession for the development costs of inventions, and thus withhold patents from drugs that are unlikely to reach the public without such protection. This gap in the patent system for drugs has created a pervasive problem in the pharmaceutical industry, causing firms to regularly screen through their drugs in R&D and discard ones with weak patent protection. The potential harm to the public from the loss of these drugs may be enormous.

Part I of the article describes how the public currently depends on patents to promote pharmaceutical innovation, and benefits from the system through the introduction of new drugs. At a time when many scholars believe that patents often do more harm than good,[2] the pharmaceutical industry is widely thought to showcase the benefits of patents.[3] Pharmaceutical companies spend hundreds of millions of dollars on clinical trials to satisfy the FDA's safety and efficacy standards, while generic drugs are exempted from those requirements and enter the market at minimal cost. Without some

[2] *See, e.g.*, BESSEN & MEURER, *supra* note 1, at 14-16; FED. TRADE COMM'N, TO PROMOTE INNOVATION: THE PROPER BALANCE OF COMPETITION AND PATENT LAW AND POLICY ch. 3, at 30, 34-41, 44, 50-55 (2003); NAT'L RESEARCH COUNCIL OF THE NAT'L ACADS., A PATENT SYSTEM FOR THE 21ST CENTURY 35-38 (Stephen A. Merrill et al. eds., 2004).
[3] *See* FED. TRADE COMM'N, *supra* note 2, ch. 3, at 14.

way to postpone competition from generics, pharmaceutical companies could not recoup their R&D costs. Under the protection of a patent, firms are able to delay generic entry for 10 to 14 years on average, providing time to profit from their R&D efforts. The promise of that reward spurs private industry to invest billions of dollars in pharmaceutical R&D each year, and those investments have yielded immense social returns in the form of valuable new medical treatments. The public pays a price for this progress, since patented drugs typically cost substantially more than generics, and consumers suffer from those high prices for the duration of the patent term. Without patents, however, the large majority of drugs likely would not be developed, and the health gains they produce might never be realized.

Part II identifies a previously unrecognized and serious defect in the patent system for pharmaceuticals: put simply, not all drugs are patentable, and there is little reason to believe that the drugs denied protection are any less valuable than patentable drugs. The theoretical point underlying this observation is straightforward. Whenever the costs of developing and commercializing an invention are both substantial and vulnerable to free-riding, as is the case with most drugs, patents can be essential for promoting those post-invention efforts. Under the novelty and non-obviousness requirements, however, patents are denied to inventions when the idea for them is not new or is obvious, regardless of whether a patent is needed for their development. Those doctrines can therefore prevent valuable inventions from reaching the public. To this author's knowledge, this article is the first to recognize that the novelty requirement can deter innovation when development and commercialization costs are high. With respect to the non-obviousness requirement, other scholars have noted the potential for such a problem,

but it has received little attention in the literature, and its implications for the pharmaceutical industry have been largely overlooked.

Section A of Part II analyzes the novelty requirement for pharmaceuticals, demonstrating how it frequently interferes with the patenting of potentially valuable drugs. In the pharmaceutical industry, merely disclosing the idea for a drug can prevent it from later being patented. Although researchers generally try to patent the new drugs they discover, current law allows seemingly insignificant disclosures to undermine the novelty of drugs, which makes it easy for researchers to unwittingly disclose their discoveries. In university laboratories, the pressure to publish often leads researchers to disclose new drugs prematurely. Private industry may be an even worse culprit, with companies regularly filing overly-broad patent applications to establish priority over large numbers of potential new drugs. As their research advances, the companies typically disclaim most of those compounds from their applications, leaving only the prior disclosure of the drugs. Practices such as these have created a significant body of potentially valuable drugs that cannot be patented.

Section B of Part II examines the non-obviousness requirement's effect as an impediment to drug patenting. Much like the novelty requirement, it denies patents to drugs before they have been developed and made available to the public. Its consequences are likely more perverse than those of the novelty standard, however, since "obvious" drugs are defined as ones that would have been reasonably expected to succeed at the time of their invention. Under the non-obviousness test, therefore, the drugs that initially look most likely to be effective are often the least likely to be patentable. The non-obviousness standard also has the ironic effect of turning progress in

the pharmaceutical sciences against itself, since it withholds patent protection from drugs based on the scientific advances that allowed researchers to identify them as ones that are likely to be effective. These counterintuitive policies embodied in the non-obviousness standard can have a significant effect on the ability of firms to patent promising new drugs.

Part III argues that the novelty and non-obviousness requirements are not just a potential threat to pharmaceutical innovation; they are actually costing the public access to valuable drugs. Since pharmaceutical companies rely on the patent system to recoup their R&D investments, they regularly screen their drug candidates during development to discard ones that appear unpatentable. In fact, the companies use redundant reviews to catch these drugs, screening through their products at least three separate times before clinical trials, and frequently abandon promising drug candidates on account of perceived weaknesses in their patent protection. It is impossible to know how many of these abandoned drugs would have proven socially valuable, given the early stage at which they are dropped from development. Nevertheless, the frequency with which this phenomenon occurs suggests that the injury to the public is substantial.

Part IV explores various policies that Congress could adopt to encourage the development of unpatentable drugs, and ultimately recommends that newly-developed drugs be guaranteed protection from generic competitors through the FDA, receiving an automatic period of market exclusivity after successfully completing clinical trials. Other possible strategies discussed are reforming the patent laws to ensure that drugs remain patentable until they are developed, and using the government to fund the development of unpatentable drugs. Those approaches both have significant drawbacks, however, since

the patent reforms might open the door to abusive patenting strategies, and a government-funded development program would be incredibly difficult to implement successfully at present. FDA-administered periods of exclusivity provide a much more sensible solution to the problem of unpatentable drugs. Unlike patent reforms, they link the reward of exclusivity to the need for that protection, since the exclusivity is given in exchange for successfully completing the FDA's clinical-trial requirements, and those requirements are themselves what make the reward of exclusivity necessary. Moreover, unlike a government-run drug-development program, Congress could easily implement the proposed FDA-administered exclusivity periods, since current law already provides for certain short delays in the approval process for generics. While those existing regulatory delay periods are rarely long enough to motivate the development of an unpatentable drug, Congress could simply lengthen them to correct this problem.

I. BACKGROUND: PATENTS AND PHARMACEUTICAL INNOVATION

Pharmaceutical innovation is often seen as the golden child of the patent system, with patents taking credit for the discovery and development of valuable new drugs that provide tremendous health benefits to the public.[4] The purpose of the patent system is to encourage socially valuable investments in R&D that firms would not otherwise make due to the profit-eroding effects of competition. In the pharmaceutical industry, firms must invest hundreds of millions of dollars in clinical trials on their drugs before they can be sold to the public, while their generic rivals are exempted from those requirements and can enter the market at low cost. Without some way to delay generic competition,

[4] *See, e.g.*, Rebecca S. Eisenberg, *The Problem of New Uses*, 5 YALE J. HEALTH POL'Y, L. & ETHICS 717, 720-21 (2005).

therefore, pharmaceutical companies would usually find it impossible to recoup their R&D investments, and would likely invest their money elsewhere. With strong patent protection, however, firms can expect to enjoy a lengthy monopoly over their drug, providing them an opportunity to profit from their investment in R&D. Although the public suffers from high prices for drugs while they are covered by a patent, most of those drugs probably would not have been developed without that protection. As a result, it is widely thought that the benefits of drug patents far outweigh their costs.

The economic function of the patent system is to promote the creation, development and commercialization of inventions.[5] Successful innovation can be of great value to society,[6] but it often requires significant investments in R&D.[7] The public relies on private industry to provide most of that investment,[8] and unless firms expect to profit from their R&D efforts, they are likely to spend their money on something else. Appropriating the returns from an R&D investment can be difficult in a competitive market, since other firms may be able to imitate successful inventions without incurring the same costs and risks.[9] The resulting price competition can undermine the original inventors' profits as competitors "free-ride" off of their efforts. The patent system is an attempt to preserve the incentive to invest in R&D that would otherwise be vulnerable to free-riding by awarding inventors temporary exclusive rights to make, use and sell their inventions, thereby protecting them from the profit-eroding effects of competition.[10]

---

[5] *See* Kenneth W. Dam, *The Economic Underpinnings of Patent Law*, 23 J. LEGAL STUD. 247, 247-48 (1994).
[6] *See* Charles I. Jones & John C. Williams, *Measuring the Social Return to R&D*, 113 QUARTERLY J. ECON. 1119 (1998).
[7] *See Industrial Research Institute's 9th Annual R&D Leaderboard*, 50 RES.-TECH. MGMT. 17 (2007).
[8] *See* CONGRESSIONAL BUDGET OFFICE, FEDERAL SUPPORT FOR RESEARCH AND DEVELOPMENT 3 (2007).
[9] *See id*. at 1.
[10] *See, e.g.*, Peter Menell & Suzanne Scotchmer, *Intellectual Property*, *in* 2 HANDBOOK OF LAW & ECONOMICS 1476 (A. Mitchell Polinsky & Steven Shavell eds. 2007); STEVEN SHAVELL, FOUNDATIONS OF

Although patent-law scholars typically focus on the role of patents in promoting inventive activity,[11] patents can be equally important in encouraging investment in the subsequent development and commercialization of inventions.[12] The idea for an invention is usually of little value to the public until it has been turned into a marketable product,[13] and the process of doing so can be both risky and expensive. Indeed, the cost and risk of bringing an invention to market is often much greater than that faced during the initial research that gave rise to the invention.[14] If competitors can produce and sell copies of the invention while avoiding its development and commercialization costs, then there may be little or no incentive for firms to ever bring that invention to market. Under these circumstances, a patent can be essential for the investment that enables the practical use of an invention – a fact known to economists for at least 100 years.[15] Even when

---

ECONOMIC ANALYSIS OF LAW 138 (2004). It is worth noting that the patent system is just one of many ways to correct for the otherwise inadequate incentives for R&D that sometimes exist in a competitive market. *See* SUZANNE SCOTCHMER, INNOVATION AND INCENTIVES 31-58 (2004).

[11] *See* Mark A. Lemley, *Ex Ante Verses Ex Post Justifications for Intellectual Property*, 71 U. CHI. L. REV. 129, 129-130 (describing the "standard economic explanation for intellectual property" as ensuring that "creators [can] recoup their investment in creating the[ir] idea[s]"); Robert Mazzoleni & Richard R. Nelson, *Economic Theories about the Benefits and Costs of Patents*, 32 J. ECON. ISSUES 1031, 1034-35 (1998) (noting that "much discussion about the benefits of patents proceeds as if motivating useful invention were the only social purpose served by patents").

[12] *See* 1 SUBCOMM. ON PATENTS, TRADEMARKS & COPYRIGHTS OF THE SENATE COMM. ON THE JUDICIARY, 85TH CONG., AN ECONOMIC REVIEW OF THE PATENT SYSTEM 36-38 (Comm. Print 1958) (prepared by Fritz Machlup) [hereinafter MACHLUP, PATENT SUBCOMM. REPORT]; Robert P. Merges, *Uncertainty and the Standard of Patentability*, 7 HIGH TECH. L.J. 1, 69-70 (1992) (arguing that "patents may spur development more than invention per se").

[13] *See* WILLIAM J. BAUMOL, THE FREE-MARKET INNOVATION MACHINE: ANALYZING THE GROWTH MIRACLE OF CAPITALISM 10 (2002).

[14] *See* MACHLUP, *supra* note 12 at 36-37; Edmund W. Kitch, *The Nature and Function of the Patent System*, 20 J.L. & ECON. 265, 276-77 (1977).

[15] *See id*. The traditional economic justification for patents likely always encompassed the promotion of development and commercialization efforts in addition to inventive activity. *See* F.M. SCHERER, INDUSTRIAL MARKET STRUCTURE AND ECONOMIC PERFORMANCE 440-41 (2d ed., F.M. Scherer ed. 1980). The idea that patents encourage post-invention efforts is now often associated with Edmund Kitch's "prospect" theory of patents. *See, e.g.*, Lemley, *supra* note 11; John F. Duffy, *Rethinking the Prospect Theory of Patents*, 71 U. CHI. L. REV. 439, 439-40 (2004). In his seminal 1977 article, *The Nature and Function of the Patent System*, Kitch argued that the patent system benefits society not just by promoting R&D investments, but also by enabling patent holders to coordinate post-invention investments efficiently, and thus avoiding wasteful or duplicative R&D. *See* Kitch, *supra* note 14. Much of Kitch's observation about patents assumes efficient licensing, *see* Menell & Scotchmer, *supra* note 10, at 1501-03, and his

patents are unnecessary for motivating the creation of an invention, therefore, they can still be critical for encouraging the subsequent investment in its development.

Of course, not all inventions need a patent to incent their development and commercialization.[16] In many cases the costs and risks of getting an invention to market are relatively small, and the inherent lead-time advantage that the inventors will enjoy over competitors is sufficient for them to recoup their R&D investments.[17] In other cases patents are unnecessary for motivating post-invention spending because those investments are not vulnerable to free-riding. For example, a firm might be willing to build an expensive new manufacturing plant to produce an unpatented invention because competitors would have to make the same investment in building their own plant before they could launch an imitation product.[18] Additionally, on some occasions the underlying invention does not need a patent because the efforts to develop and commercialize it give rise to their own patentable invention,[19] which can make it difficult for competitors to capitalize on the innovative firm's post-invention expenses.[20] In any

---

argument has proven controversial. *See e.g.*, *id*.; Duffy, *supra*; Mark F. Grady & Jay I. Alexander, *Patent Law and Rent Dissipation*, 78 VA. L. REV. 305 (1992); Lemley, *supra* note 11; Dongal G. McFetridge & Douglas A. Smith, *Patents, Prospects, and Economic Surplus: A Comment*, 23 J. L. & Econ. 197 (1980); Robert P. Merges & Richard R. Nelson, *On the Complex Economics of Patent Scope*, 90 COLUM. L. REV. 839, 842-44, 908-16 (1990); Arti Kaur Rai, *Regulating Scientific Research: Intellectual Property Rights and the Norms of Science*, 94 NW. U.L. REV. 77, 120-135 (1999). This debate is largely unrelated to the traditional economic justification for patents, which is that without a patent system the threat of competition deters investment in R&D.

[16] *See* WESLEY M. COHEN ET AL., PROTECTING THEIR INTELLECTUAL ASSETS: APPROPRIABILITY CONDITIONS AND WHY U.S. MANUFACTURING FIRMS PATENT (OR NOT) (Nat'l Bureau of Econ. Research, Working Paper No. 7552, 2000), *available at* http://www.nber.org/papers/w7552; Mazzoleni & Nelson, *supra* note 11, at 1047-48.

[17] *See* COHEN ET AL., *supra* note 16, at tbl.1; Mazzoleni & Nelson, *supra* note 11, at 1041.

[18] *See* Kitch, *supra* note 14, at 276; F. M. Scherer, *Pharmaceutical Innovation*, AEI-Brookings Joint Center Working Paper No. 07-19, at 27-28 (Jun. 2007), *at* http://ssrn.com/abstract=902395.

[19] *See, e.g.*, Suzanne Scotchmer & Stephen M. Maurer, *Innovation Today: A Public-Private Partnership*, *in* INNOVATION AND INCENTIVES, *supra* note 10, at 243-44.

[20] *But cf. Note, The Disclosure Function of the Patent System (or Lack Thereof)*, 118 HARV. L. REV. 2007, 2015-16 (2005) (noting that patent protection is often ineffective for process innovations because detecting infringement can be difficult); Eisenberg, *supra* note 4, at 721 (explaining that "patents have remained unavailable for data").

of these situations, the absence of patent protection for an invention may not deter its development.

For some inventions, however, patents do play an essential role in promoting their development and commercialization, and drugs are a clear example.[21] Pharmaceutical companies spend somewhere between $800 million and $1.2 billion on R&D for each new drug that reaches the market.[22] Roughly half of that money is spent satisfying the FDA's clinical-trial requirements to establish the safety and efficacy of new drugs,[23] producing data that cannot be protected with patents.[24] Meanwhile, generics are exempted from the FDA's clinical-trial requirements, entering the market based on the clinical-trial data submitted by the pharmaceutical company.[25] As a result, generic-drug manufacturers spend on average only about two million dollars on the approval process.[26] Once they are on the market, those drugs dramatically reduce sales of (and profits from) the name-brand drugs they imitate.[27] Pharmaceutical companies therefore rely on a lengthy period of market exclusivity to recoup their investments in developing new drugs. With strong patent protection, they are usually able to keep generics off the

[21] *See* Dan L. Burk & Mark A. Lemley, *Policy Levers in Patent Law*, 89 VA. L. REV. 1575, 1676-77 (2003).
[22] *See* Joseph A. DiMasi et al., *The Price of Innovation: New Estimates of Drug Development Costs*, 22 J. HEALTH ECON. 151, 180-83 (2003); Joseph A. DiMasi & Henry G. Grabowski, *The Cost of Biopharmaceutical R&D: Is Biotech Different?*, 28 MANAGERIAL & DECISION ECON. 469 (2007); Christopher P. Adams & Van V. Brantner, *Estimating the Cost of Drug Development: Is it Really $802 Million?*, 25 HEALTH AFFAIRS 420 (2006). This estimate includes the research and development costs of failed drug candidates as well as the opportunity costs of the investments.
[23] *See* DiMasi et al., *supra* note 22.
[24] *See* Eisenberg, *supra* note 4, at 721-22.
[25] *See* 21 U.S.C. § 355(j)(8)(B).
[26] *See Big Generic Pharma*, ECONOMIST, vol. 376, Jul. 30, 2005, at 58.
[27] *See* CONGRESSIONAL BUDGET OFFICE, U.S. CONGRESS, RESEARCH AND DEVELOPMENT IN THE PHARMACEUTICAL INDUSTRY 16 (2006); Richard G. Frank & Erica Seiguer, *Generic Drug Competition in the US*, BUSINESS BRIEFING: PHARMATECH 2003, at 56-58.

market for somewhere between 10 and 14 years,[28] and will invest hundreds of million of dollars in R&D in anticipation of this reward.[29] For this reason, scholars often view drug development as "the paradigm of patents spurring innovation."[30]

Relying on the patent system to promote pharmaceutical innovation has its costs, of course, since patents allow manufacturers to charge premium prices for their drugs.[31] Although pharmaceutical companies sink vast sums of money into the R&D of new drugs, the actual costs of manufacturing those drugs is usually quite low.[32] Generic drugs are sold at prices that reflect these lower production costs, whereas patented drugs are priced much higher.[33] When a drug is patented, therefore, some consumers who would be willing to buy it at the generic price are forced out of the market, and they must wait until the patent on the drug expires before benefiting from its use. Economists refer to this harm as deadweight loss, and it is a problem inherent in the patent system.[34] With pharmaceuticals, the deadweight loss caused by patent protection is especially troubling

---

[28] *See* Henry G. Grabowski & Margaret Kyle, *Generic Competition and Market Exclusivity Periods in Pharmaceuticals*, 28 MANAGERIAL & DECISION ECON. 491 (2007); Henry G. Grabowski & John M. Vernon, *Effective Patent Life in Pharmaceuticals*, 19 INT'L J. TECH. MGMT. 98, 109-117 (2000).

[29] *See* DiMasi et al., *supra* note 22; Carmelo Giaccotto et al., *Drug Prices and Research and Development Investment Behavior in the Pharmaceutical Industry*, 48 J.L. & ECON. 195, 212 (2005); F. M. Scherer, *The Link Between Gross Profitability and Pharmaceutical R&D Spending: An Analysis that Answers the Question: What does the Pharmaceutical Industry Really do with its Profits?*, 20 HEALTH AFF. 216, 220 (2001).

[30] John H. Barton & Ezekiel J. Emanuel, *The Patents-Based Pharmaceutical Development Process: Rationale, Problems, and Potential Reforms*, 294 J. AM. MED. ASS'N 2075, 2077 (2005); *see also* FED. TRADE COMM'N, *supra* note 2, ch. 3, at 14 (concluding that pharmaceutical innovation "showcases the patent system's benefits"); *cf.* JAFFE & LERNER, *supra* note 1, at 39-41.

[31] *See, e.g.*, SCOTCHMER, *supra* note 10, at 34-39.

[32] *See* James W. Hughes et al., *"Napsterizing" Pharmaceuticals: Access, Innovation , and Consumer Welfare*, NBER Working Paper 9229, at 6 (2002).

[33] *See* Hughes et al., *supra* note 32, at 6 (noting that "the ratio of price to marginal cost for branded drugs with patent protection is about 6:1").

[34] There are alternative mechanisms for promoting innovation that avoid this deadweight loss problem, such as a rewards system or direct government investment in R&D. *See, e.g.*, SCOTCHMER, *supra* note 10, at 31-58; Steven Shavell & Tanguy Van Ypersele, *Rewards Verses Intellectual Property Rights*, 44 J.L. & ECON. 525 (2001). In the context of pharmaceuticals, another way to minimize the deadweight loss problem caused by patents is through government subsidies for (or provision of) prescription-drug insurance – a policy that operates much like a reward system.

because some people must forgo the use of drugs that would improve their health, and sometimes even save their lives.[35]

Although the temporary high prices that result from patent protection are a significant problem, the benefits of the patent system can outweigh these costs. The public may suffer for a time from the higher prices charged for a patented invention, but that harm is necessarily smaller than the injury that would result if no one ever created or developed that invention in the first place, or if it would have taken much longer for the invention to reach the public. As a rule of thumb, therefore, patents are socially desirable when, in their absence, the public would not otherwise benefit from the invention or there would be a substantial delay in the public's receipt of that benefit.[36]

The pharmaceutical industry is probably the best example of where patents are socially desirable under this rule of thumb, since patents appear to be a prerequisite for most pharmaceutical innovation.[37] Given their high R&D costs compared to those of their generic rivals, pharmaceutical companies rely on lengthy periods of market exclusivity – normally 10 or more years for the drugs currently developed – to support

[35] *See* Arti K. Rai, *The Information Revolution Reaches Pharmaceuticals: Balancing Innovation Incentives, Cost, and Access in the Post-Genomic Era*, 2001 U. ILL. L. REV. 173, 187-88 (2001).

[36] This rule of thumb is more of a heuristic than an absolute economic principle. An exact account of the social welfare consequences of a patent grant would have to consider the numerous positive and negative externalities of issuing a patent, including its effect on wasteful and duplicative R&D spending; the administrative and enforcement costs of patents; reduced spending on trade secrecy (and perhaps increased labor mobility from less reliance on employee non-competition covenants); the potential stifling of related innovation or improvements due to overly-broad patent claims, unclear patent boundaries, high licensing costs, anti-commons, and patent thickets; R&D spillovers from patents; and reducing licensing costs in comparison to trade secrets. Although these secondary economic effects can be important, they are often hard to calculate and, at least with respect to pharmaceuticals, they do not appear to overwhelm the social value of the inventions brought forth from patent protection. *See infra* text accompanying notes 44-47; BESSEN & MEURER, *supra* note 1, at 88-89.

[37] *See, e.g.*, NAT'L RESEARCH COUNCIL, *supra* note 2, at 41; Edwin Mansfield, *Patents and Innovation: An Empirical Study*, 32 MANAGEMENT SCI. 173, 174-75 (1986).

their investments in bringing drugs to market.[38] Not surprisingly, therefore, firms in the industry consistently report that patent protection is essential for their efforts to discover and develop new drugs.[39] Moreover, it is well known that pharmaceutical companies generally refuse to develop a new drug unless they have strong patent protection over it.[40] Indeed, drug researchers who work in government and academia report that when they are looking for a partner in private industry to fund the development of a new drug, it is almost impossible to attract interest unless the drug is patented.[41]

Some scholars even worry that that the patent system may be too effective at promoting pharmaceutical innovation,[42] although the available evidence indicates that society's investment in pharmaceutical R&D continues to generate substantial positive returns. In theory, the patent system could be harming the public by causing wasteful and duplicative R&D in "patent races."[43] In the case of pharmaceuticals, however, numerous economic studies have found that the social benefits produced by new medical

---

[38] *See infra* notes 337. *Cf.* Henry Grabowski, *Are the Economics of Pharmaceutical Research and Development Changing? Productivity, Patents and Political Pressures*, 22 PHARMACOECONOMICS 15 (Suppl. 2), 21 (2004).

[39] For a concise summary of this evidence, *see* F. M. SCHERER, THE POLITICAL ECONOMY OF PATENT POLICY REFORM IN THE UNITED STATES 6-9, 13 (Dynamics of Inst. & Markets in Eur., Intell. Prop. Rts. Working Paper No. 26, Dec. 2006), *available at* http://www.dime-eu.org/node/365.

[40] *See, e.g.*, C. Merle Crawford, *Defining the Charter for Product Innovation*, *in* GENERATING TECHNOLOGICAL INNOVATION 175 (Edward B. Roberts ed. 1987); Peter Gwynne & Gary Heebner, *Laboratory Technology Trends: Drug Discovery: 4 Protecting the Assets*, 297 SCI. 2083, 2086 (2002); Lester A. Mitscher & Apurba Dutta, *Contemporary Drug Discovery*, *in* DRUG DISCOVERY AND DEVELOPMENT 104, 115 (Mukund S. Chorghade ed. 2006); BERNICE SCHACTER, THE NEW MEDICINES: HOW DRUGS ARE CREATED, APPROVED, MARKETED, AND SOLD 52 (2006).

[41] *See* Jason Owen-Smith & Walter W. Powell, *To Patent or Not: Faculty Decisions and Institutional Success at Technology Transfer*, 26 J. TECH. TRANSFER 99, 108 (2001); Letter from Harold E. Varmus, Director of the National Institutes of Health, to James Love, Director of the Consumer Project on Technology (Oct. 19, 1999), *at* http://www.cptech.org/ip/health/sa/varmusletteroct19.html.; Telephone Interview with Brian J. Druker, M.D., Professor of Medicine at the Oregon Health & Science University Cancer Institute, JELD-WEN Chair of Leukemia Research (Dec. 5, 2006) (on file with author).

[42] *See* WILLIAM M. LANDES & RICHARD A. POSNER, THE ECONOMIC STRUCTURE OF INTELLECTUAL PROPERTY LAW 315-16 (2003).

[43] *See, e.g.*, MACHLUP, *supra* note 12, at 50-51.

technologies significantly outweigh the costs of society's investment in medical R&D.[44] According to one estimate, new drug launches in the United States increase the population's average annual life expectancy by about one week, leading to a cost-effectiveness ratio for pharmaceutical R&D spending of $6750 for each additional year of life saved.[45] Since most studies put the value of a year of life at $75,000 to $150,000,[46] the social return on pharmaceutical R&D investments appears to be extraordinarily high.[47] This is not to say that all investments in pharmaceutical R&D are beneficial, since some of that spending goes toward drugs that fail to complete the FDA's clinical-trial requirements,[48] drugs that offer little or no therapeutic advantage over existing drugs,[49] and sometimes even drugs that do more harm than good,[50] such as the now-

---

[44] *See, e.g.*, David M. Cutler & Mark McClellan, *Is Technological Change In Medicine Worth It?*, 20 HEALTH AFFAIRS 11, 23 (2001); Hughes et al., *supra* note 32, at 10-14; Frank R. Lichtenberg, *The Benefits to Society of New Drugs: A Survey of the Econometric Evidence*, *in* ENGAGING THE NEW WORLD: RESPONSES TO THE KNOWLEDGE ECONOMY 43 (Bhajan S. Grewal & Margarita Kumnick eds. 2006); Kevin M. Murphy & Robert H. Topel, *The Value of Health and Longevity*, 114 J. POL. ECON. 871, __ (2006); FRANK A. SLOAN & CHEE-RUEY HSIEH, EFFECTS OF INCENTIVES ON PHARMACEUTICAL INNOVATION 5-9 (Jul. 27, 2006), *at* http://www.oberlin.edu/economic/Papers/HealthConf/Sloan.pdf. Another reason to doubt that patent races in the pharmaceutical industry undermine the social welfare produced by innovation is that drug manufacturers often appropriate only a small fraction of the social surplus arising from their new technologies. *See* Tomas J. Philipson & Anupam B. Jena, *Surplus Appropriation from R&D and Health Care Technology Assessment Procedures*, NBER Working Paper W12016, Feb. 2006, *at* http://ssrn.com/abstract=881250.

[45] *See* Frank R. Lichtenberg, *The Impact of New Drug Launches on Longevity: Evidence from Longitudinal, Disease-Level Data from 52 Countries, 1982-2001*, 5 INT'L J. HEALTH CARE FINANCE & ECON. 47, 71 (2005); *see also* Pierre-Yves Cremieux et al., *Pharmaceutical Spending and Health Outcomes*, *in* PHARMACEUTICAL INNOVATION: INCENTIVES, COMPETITION, AND COST-BENEFIT ANALYSIS IN INTERNATIONAL PERSPECTIVE (Frank A. Sloan & Chee-Ruey Hsieh eds. 2006) (concluding that "pharmaceutical spending is a worthwhile investment with high rates of return"); Chee-Ruey Hsieh et al., *Pharmaceutical Innovation and Health Outcomes: Empirical Evidence from Taiwan*, *in* PHARMACEUTICAL INNOVATION: INCENTIVES, COMPETITION, AND COST-BENEFIT ANALYSIS IN INTERNATIONAL PERSPECTIVE 258 (Frank A. Sloan & Chee-Ruey Hsieh eds. 2006) (concluding that the incremental cost-effectiveness ratio of new drug launches in Taiwan is $1,704 per life year saved); Frank R. Lichtenberg, *The Impact of New Drugs on US Longevity and Medical Expenditure, 1990-2003: Evidence from Longitudinal, Disease-Level Data*, 97 AM. ECON. REV. 438, 442 (2007) (finding that for the United States' investment in pharmaceuticals, the net cost for each life-year saved before age 75 is $15,974).

[46] *See* DAVID M. CUTLER, YOUR MONEY OR YOUR LIFE: STRONG MEDICINE FOR AMERICA'S HEALTHCARE SYSTEM 16 (2004).

[47] *See supra* note 44.

[48] *See* DiMasi et al., *supra* note 22.

[49] *See* Rai, *supra* note 35, at 205-06.

infamous pain reliever Vioxx®.[51] On the whole, however, society's investments in discovering and developing new drugs seem to yield substantial net benefits.

The discussion above demonstrates why the case for the patent system is at its strongest in the pharmaceutical industry, since innovation in the field is incredibly valuable to society and most of it would not occur without the patent system.[52] Indeed, it is considered "well established" that the availability of patent protection for drugs improves social welfare.[53] This is not to say that the patent system is perfect; no one questions that the public suffers greatly from high drug prices. At the moment, however, the public depends on the patent system to promote pharmaceutical innovation, and usually benefits when the system is successful in that task.

II. THE PATENT STANDARDS AND THE DEVELOPMENT COSTS OF DRUGS

When scholars recount the story of pharmaceutical innovation as the patent system's great success story, they focus on how patents are a necessary incentive for the discovery and development of most drugs. It is often assumed that patent protection is always available to promote the development of drugs that need it.[54] That assumption is wrong. When the idea for a drug is insufficiently new or inventive, it cannot be patented, even when that drug has not yet been proven safe and effective in clinical trials, and thus

---

[50] *See* Jerry Avorn, *Dangerous Deception – Hiding the Evidence of Adverse Drug Effects*, 355 NEW ENG. J. MED. 2169, 2169-70 (2006).
[51] *See* Margaret Gilhooley, *Vioxx's History and the Need for Better Procedures and Better Testing*, 37 SETON HALL L. REV. 941 (2007).
[52] *See* SCHERER, *supra* note 39.
[53] *See* NAT'L RESEARCH COUNCIL, *supra* note 2, at 41.
[54] *See, e.g.*, RICHARD A. EPSTEIN, OVERDOES: HOW EXCESSIVE GOVERNMENT REGULATION STIFLES PHARMACEUTICAL INNOVATION 58 (2006) (noting that "the overall [patent] system tends to be reliable, especially for pharmaceutical patents").

cannot be approved by the FDA for sale to the public.[55] This section explores the gap in protection left by this rule, explaining how the novelty and non-obviousness requirements, two of the three basic standards of patentability,[56] operate to prevent valuable drugs from being patented before they have been developed for public use.

At a more general level, this section notes that whenever the post-invention costs of developing and commercializing an invention are substantial and vulnerable to free-riding by competitors, the novelty and non-obviousness requirements can deny patents to inventions that are unlikely to reach the public without that protection. This problem arises in the pharmaceutical industry because of the need for safety and efficacy testing, which forces pharmaceutical companies to invest hundreds of millions of dollars in clinical trials while generics can enter the market almost freely. Although the analysis in this section is limited to pharmaceuticals, it is *possible* that similar problems occur in

[55] This observation is relevant to the burgeoning literature on "reverse payment" settlements of drug patent litigation, discussing settlements where pharmaceutical companies pay the generic manufacturer challenging their patent to delay releasing its product until near the end of the patent term. *See* Bureau of Competition, Federal Trade Commission, Agreements Filed with the Federal Trade Commission under the Medicare Prescription Drug, Improvement, and Modernization Act of 2003: Summary of Agreements Filed in FY 2006, at 4-5 (Jan. 2007). These agreements have been criticized for enabling pharmaceutical companies to "pay for delays" in generic competition, which forces consumers to pay higher prices for drugs. C. Scott Hemphill, *Paying For Delay: Pharmaceutical Patent Settlement as a Regulatory Design Problem*, 81 N.Y.U. L. REV. 1553 (2006); *see also* Federal Trade Commission (FTC), *Competition in the Pharmaceutical Marketplace: Antitrust Implications of Patent Settlements*, Prepared Statement before the Committee on the Judiciary, United States Senate, at 10-19 (May 24, 2001). Such criticisms presume that if the patent on a drug is invalid, then the public is best served by allowing generics to enter. In reality, the patent standards for pharmaceuticals correspond poorly to whether patent protection is necessary for a drug's development. *See infra* text accompanying notes 77-79, 165-168. To analyze the social-welfare consequences of these settlement agreements, therefore, attention should be paid to the grounds upon which the patent is being challenged, and whether that patent was likely necessary for the drug's development.

[56] Inventions must be new, not obvious and useful to be patented. *See* 35 U.S.C. §§ 101-103. Unlike the novelty and non-obviousness standards, the utility requirement cannot alone deny patent protection to a valuable drug, since any drug lacking "utility" is not valuable. In fact, the utility requirement is often considered perfunctory, although it has some bite with pharmaceutical patents, *see* STEPHEN A. BECKER, PATENT APPLICATIONS HANDBOOK § 6:31 (2006), forcing inventors to delay filing a patent on a drug until they possess sufficient evidence to demonstrate its claimed utility. *See infra* notes 91-94.

other industries.[57] Of course, any such extension of the analysis below must be done with care. One might assume that the same problems that arise for the traditional pharmaceuticals discussed below also arise for newer biologic drugs (*i.e.*, large-molecule drugs such as human growth hormone), since both are subject to the same safety and efficacy standards.[58] There is no regulatory path for generics in the biologic industry,[59] however, and thus no need for patents to prevent generics from using another firm's clinical-trial data to enter the market.[60] Given the sensitivity in the analysis to industry variations, this section focuses only on patent protection for traditional pharmaceuticals, even though the thesis can be stated more generally as applying whenever post-invention costs are significant and subject to free-riding.

A. The Novelty Requirement

More than any of the other doctrines in patent law, the novelty requirement epitomizes the patent system's failure to adequately promote pharmaceutical innovation by ignoring the development and commercialization costs of inventions. This failure is particularly notable because the novelty requirement is probably the least controversial rule in patent law, stating only that an invention must be new to be patented. In the pharmaceutical industry, this rule means that a drug cannot be patented if the idea for it was previously disclosed to the public; no exception is made for when the disclosed drug has not yet been tested in clinical trials, and thus has not been approved by the FDA.

[57] Two other industries where the novelty and non-obviousness requirements *might* have similar effects are agricultural chemicals and medical equipment, since both of those industries are governed by a regulatory regime similar to the one for drugs. *See* 7 U.S.C. § 136; 21 U.S.C. § 360.
[58] *See* PETER BARTON HUTT ET AL., FOOD AND DRUG LAW: CASES AND MATERIALS 624-734 (3rd 2007).
[59] *See* Richard G. Frank, *Regulation of Follow-on Biologics*, 357 NEW ENG. J. MED. 841, 841-43 (2007).
[60] If firms in the biologic industry are expecting Congress to change these regulations soon to permit generic entry, the problems with the novelty and novelty requirements discussed below might be occurring for biologics even though they do not yet face generic competition.

This problem arises with surprising frequency in the industry, as it is not uncommon for scientific publications to disclose a drug in a manner that later prevents it from being patented. Courts exacerbate the situation by invaliding drug patents on the basis of seemingly trivial disclosures, often made before anyone recognized the value of the drug or knew enough about it to file a patent. As a result, the novelty requirement makes it easy for valuable drugs to become unpatentable before they have been developed for public use.

Part one of this section explains how the novelty requirement operates with respect to pharmaceutical inventions, denying patent protection to drugs on the ground that the idea for them was previously disclosed in some manner. Part two examines how the courts exacerbate this problem with an expansive interpretation of novelty that makes it easy for researchers to undermine the patentability of the drugs they discover. Part three discusses how drug researchers at universities and in private industry sometimes fall into this trap, disclosing drugs prematurely such that they cannot later be patented.

1. The Novelty Standard for Drugs

Only new drugs can be patented, and the patent system judges novelty based on whether the idea for an invention is new, not whether the public has access to the invention. It is well accepted that the disclosure of an idea for a drug can prevent it from later being patented, even if that drug is not yet available to the public. Under these circumstances the patent system offers no incentive for the development of drugs into FDA-approved products.

The novelty requirement provides that an invention is only patentable if it is a new idea.[61] Inventions that have been freely disclosed to the public are considered part of the "public domain," and are "no longer patentable by anyone."[62] The novelty doctrine therefore precludes the patenting of any invention that "was known or used by others in this country, or patented or described in this or a foreign country, before the invention thereof by the applicant for patent."[63] The rule also states that once an invention is disclosed to the public, either by being "patented or described in a printed publication in this or a foreign country or in public use or on sale in this country," the inventors have just one year to submit a patent application on it.[64] After that one-year grace period, their invention belongs to the public.[65] Pursuant to the novelty doctrine, therefore, a patented invention that was disclosed to the public before the patentees invented it, or disclosed more than a year before they filed their patent application, is "anticipated" by the prior disclosure, and the patent is invalid.

The economic rationale for the novelty requirement is so widely accepted among patent-law scholars that it is almost canonical;[66] if an invention is not new, then it is

---

[61] *See* 35 U.S.C. § 101.
[62] In re Hall, 781 F.2d 897, 898 (Fed. Cir. 1986).
[63] 35 U.S.C. § 102(a).
[64] 35 U.S.C. § 102(b).
[65] *Id*. For the sake of simplicity, this paper refers to §§ 102(a) and (b) together as the novelty requirement, although they are usually treated separately. *See, e.g.*, DONALD S. CHISUM, 1 CHISUM ON PATENTS § 3.01 (2006). Section 102(a) prohibits someone from patenting an invention if, before she conceived of it, it had been invented and disclosed to the public by someone else. Section 102(b) prohibits anyone from patenting an invention that was disclosed by *anyone* more than one year before the patent application was filed, including by a subsequent inventor or even the patent applicant herself. As a result, § 102(b) is often referred to as a "statutory bar" or "loss of right" provision, and it encourages inventors to file their patent applications early. *See* ROBERT PATRICK MERGES & JOHN FITZGERALD DUFFY, PATENT LAW AND POLICY: CASES AND MATERIALS 541-42 (3d ed. 2002). At the same time, § 102(b) also acts as a more administrable version of the novelty requirement. For purposes of this paper, the distinction between § 102(a) and § 102(b) is usually irrelevant.
[66] *See* Duffy, *supra* note 15, at 502; Merges, *supra* note 12, at 12. Scholars sometimes question certain details of the novelty doctrine, but rarely the basic rule. *See, e.g.*, Rebecca S. Eisenberg, *Analyze This: A Law and Economics Agenda for the Patent System*, 53 VAND. L. REV. 2081, 2088-91 (2000).

presumed that the public already has access to it, and thus there is no reason to issue a patent for it. The patent system is designed to reward only those inventions that the public would not have received absent the inducement of a patent. Underlying the novelty requirement, therefore, is the assumption that disclosing an invention to the public provides free access to its benefits, making patent protection unnecessary.[67] This assumption is so deeply entrenched in the literature on patents that scholars have defined the very purpose of the patent system as "the promotion of new and improved works,"[68] and the novelty requirement is said "to lie at the heart of the patent system."[69] The Supreme Court has even stated that the novelty bar is an "inherent requisite[] in a patent system which by constitutional command must 'promote the Progress of . . . useful Arts,'"[70] and intellectual-property scholars routinely cite this proposition with approval.[71] There appears to be near uniform agreement that the novelty rule is *always* a sensible limit on the government's authority to grant patents, regardless of the invention at issue.

This consensus view on the novelty requirement ignores the crucial role that patents sometimes play in encouraging the development and commercialization of inventions, since the doctrine bars the patenting of old ideas for inventions regardless of

---

[67] *See* Eisenberg, *supra* note 66, at 2088 ("Granting patents on technologies that are not new would impose the social costs of monopolies without the counterveiling benefits of promoting development and introduction of welfare-enhancing inventions."); Merges, *supra* note 12, at 12-13 ("The logic behind [the novelty requirement] is fairly straightforward," since if "information is already in the public domain when the 'inventor' seeks to patent it[,] society has no need to grant a patent to get this information").

[68] Menell & Scotchmer, *supra* note 10, at __; *see also* Barton & Emanuel, *supra* note 30, at 2076 (stating that the novelty requirement "ensure[s] innovation by precluding patents for something already invented").

[69] CHISUM, *supra* note 65, at § 3.01; *see also* MACHLUP, PATENT SUBCOMM. REPORT, *supra* note 12, at 3.

[70] Graham v. John Deere Co., 383 U.S. 1, 5-6 (1966) (quoting U.S. CONST. art. I, § 8, cl. 8); *see also* Bonito Boats, Inc. v. Thunder Craft Boats, Inc., 489 U.S. 141, 146 (1989).

[71] *See, e.g.*, Margo A. Bagley, *Patently Unconstitutional: The Geographic Limitation on Prior Art in a Small World*, 87 MINN. L. REV. 679, 679-91 (2003); John H. Barton, *Non-Obviousness* 43 IDEA 475, 487-88, 96 (2003); Jim Chen, *The Parable of the Seeds: Interpreting the Plant Variety Protection Act in Furtherance of Innovation Policy*, 81 NOTRE DAME L. REV. 105, 116-17 (2005); Robert Patrick Merges & Glenn Harlan Reynolds, *The Proper Scope of the Copyright and Patent Power*, 37 HARV. J. LEGIS. 45, 57-58 (2000).

whether a patent is needed for those inventions to reach the public. As discussed in Part I, it is well known that patents are sometimes necessary for motivating the efforts to develop an invention into a marketable product.[72] A patent is only awarded in exchange for the creation and disclosure of inventions,[73] however, not for their subsequent development or commercialization.[74] Scholars seem to have assumed that if an invention needs patent protection to be made available to the public, then it will in fact be patentable.[75] Under the novelty doctrine, however, the investment necessary to develop and commercialize an invention is irrelevant to its patentability. Once the idea for an invention ceases to be novel, the incentive provided by the patent system for bringing it to market disappears, no matter how critical that incentive might be. Although this point may seem obvious, to this author's knowledge it has not been made before now.[76]

This aspect of the novelty requirement takes on great importance in the pharmaceutical industry, where new drugs can cease to be "novel" inventions long before they have undergone the clinical trials needed to establish their medicinal value, and thus can become unpatentable before the public ever gains access to them. Unless a new drug is proven safe and effective in clinical trials, neither the FDA nor the medical community will accept its use in the practice of medicine.[77] A publication that merely discloses the

---

[72] *See supra* text accompanying notes 12-15.
[73] *See* Pfaff v. Wells Elecs., Inc., 525 U.S. 55, 63 (1998).
[74] *See* Kitch, *supra* note 14, at 276-77.
[75] *See, e.g.*, F. Scott Kieff, *Property Rights and Property Rules for Commercializing Inventions*, 85 MINN. L. REV. 697, 714 (2001); Kitch, *supra* note 14, at 284.
[76] A related point about the novelty requirement, made by William Kingston, is that the patent system fails to adequately promote innovation when final commercialized products bear little relationship to individually patented inventions, since the link between the patent grant and the incentive to commercialize a product is then weak. *See* William Kingston, *The Unexploited Potential of Patents*, *in* DIRECT PROTECTION OF INNOVATION 9, 12-14, 20-21, 30-32 (William Kingston ed. 1987). This view leads Kingston to conclude that patents fail to adequately promote innovation in most fields other than chemicals and pharmaceuticals, where the "invention-innovation link is . . . strong." *Id*. at xi, 12-13, 90.
[77] *See* HUTT ET AL., *supra* note 58, at 624-734 (detailing the FDA approval process for new drugs); Evidence-Based Medicine Working Group, *Evidence-Based Medicine: A New Approach to Teaching the*

idea for a new drug is rarely enough for the public to benefit from that drug's discovery. Nonetheless, such a disclosure can prevent anyone else from later patenting that same drug, since it is no longer a novel invention.[78] Once a year has passed from the date of publication, not even the scientists who first invented the drug can patent it, and their invention falls permanently into the public domain.[79] The novelty requirement therefore creates a substantial gap in the scope of patent protection for pharmaceuticals, wherein a new drug can become unpatentable before it has been tested in clinical trials.

A recent Federal Circuit decision aptly demonstrates this problem, showing how the novelty requirement can render a drug unpatentable prior to clinical trials, and thus before the public can benefit from its use.[80] The case involved the analgesic drug Ultracet®, a combination of two older drugs that interact synergistically to provide added pain relief with a lower incidence of side-effects.[81] The idea of combining the two drugs first appeared in a 1972 publication, but was mentioned just briefly[82] and went unnoticed by the medical community.[83] Physicians did not begin prescribing the combination until

---

Practice of Medicine, 268 J. AM. MED. ASS'N 2420, 2420 (1992) (noting that "[i]t is now accepted [by physicians] that virtually no drug can enter clinical practice without a demonstration of its efficacy in clinical trials").

[78] *See* 35 U.S.C. § 102(a). For examples of such cases, *see infra* notes 99-104.

[79] *See* 35 U.S.C. § 102(b).

[80] *See* Ortho-McNeil Pharm., Inc. v. Caraco Pharm. Labs., Ltd., 476 F.3d 1321, 1324-25 (2007) (recounting how a prior publication forced Ortho-McNeil to narrow its patent on Ultracet® to such an extent that it could no longer prevent generic companies from entering the market).

[81] Ultracet® is a fixed-dose combination of acetaminophen and tramadol.

[82] The publication that first disclosed the idea of combining tramadol and acetaminophen was the original 1972 patent on tramadol, which mentioned it in a long list of many other drug combinations involving tramadol. *See* U.S. Pat. 3,652,589 (issued Mar. 28, 1972). The patent did not claim the tramadol-acetaminophen combination as part of the invention. *Id.*

[83] As reported in PubMed, the first peer-reviewed article to discuss using tramadol and acetaminophen combined as an analgesic (in animal experiments) was published in 1996. *See* Ronald J. Tallarida and Robert B. Raffa, *Testing for Synergism Over a Range of Fixed Ratio Drug Combinations: Replacing the Isobologram*, 58 LIFE SCI. PL-23 (1996). One of the authors of the article, Robert Raffa, is a named inventor in the patent at issue in the Ultracet® case. *See* U.S. Pat. 5,336,691 (issued Aug. 9, 1994).

2001,[84] after a pharmaceutical company established its safety and efficacy and received FDA approval to market it under the tradename Ultracet®.[85] That company, which was unaware of the prior disclosure in the 1972 publication,[86] received its own patent on the combination in 1994,[87] and thereafter funded clinical trials necessary for regulatory approval. Once the 1972 publication came to light, however, it was unable to prevent generic-drug companies from entering the market.[88] Although the benefits of Ultracet® were unknown to the public before the pharmaceutical company patented it and established its safety and efficacy, the idea for the combination was not new, and, for better or worse, the novelty requirement "assure[s] that ideas in the public domain remain there for the free use of the public."[89]

2. Turning the Novelty Requirement into a Trap for the Unwary

Although there is a strong financial incentive for drug researchers to secure patent rights over their inventions, the novelty requirement contains several pitfalls that make it

[84] Based on a search in PubMed, the first medical-journal article to recommend combining tramadol and acetaminophen was published in 2001, just after FDA approval. *See* R. B. Raffa, *Pharmacology of Oral Combination Analgesics: Rational Therapy for Pain*, 26 J. CLINICAL PHARMACY AND THERAPEUTICS 257 (2001) (authored by one of the named inventors in the Ultracet® patent); *cf.* D. J. R. Duthie, *Remifentanil and Tramadol*, 81 BRIT. J. ANAESTHESIA 51, 56 (1998); Paul A. Moore, *Pain Management in Dental Practice: Tramadol vs. Codeine Combinations*, 130 J. AM. DENTAL ASS'N 1075, 1077 (1999).

[85] Approval Letter, Application No. 21-123, Center for Drug Evaluation and Research (Aug. 15, 2001), *available at* http://www.fda.gov/cder/foi/nda/2001/21123_Ultracet_Approv.pdf.

[86] Ortho-McNeil did not learn of the reference to combining acetaminophen and tramadol in the 1972 patent disclosure until 2004, at which point it initiated a reissue proceeding with the PTO in an attempt to salvage its patent. *See* Ortho-McNeil Pharm. Inc. v. Caraco Pharm. Labs., Ltd., No. 04-CV-73698, 2005 WL 2679788, at *1 (E.D. Mich. Oct. 19, 2005). Although one might have expected Ortho-McNeil to find this reference sooner, the 1972 patent uses an obscure synonym of acetaminophen, "p-acetamino phenal," in its reference to the combination, *see* U.S. Pat. 3,652,589, and was likely overlooked for that reason.

[87] U.S. Pat. 5,336,691.

[88] Ortho-McNeil Pharm., Inc. v. Caraco Pharm. Labs., Ltd., No. 04-CV-73698, at *1 (E.D. Mich. Oct. 19, 2005), *aff'd* 476 F.3d 1321 (Fed. Cir. 2007). The first generic version of Ultracet® entered the U.S. market in late 2005, just over four years after Ortho-McNeil began selling it. *See* Press Release, Caraco Pharm. Labs. Ltd., Caraco Pharmaceutical Laboratories Ltd. Wins Appeal for Generic Ultracet (Jan. 17, 2007), *at* http://www.prnewswire.com/cgi-bin/stories.pl?ACCT=104&STORY=/www/story/01-19-2007/0004509401&EDATE=.

[89] Aronson v. Quick Point Pencil Co., 440 U.S. 257, 262 (1979).

easy for researchers to unwittingly undermine the patentability of new drugs. Cursory disclosures containing little information about a drug are often enough to later prevent it from being patented. In fact, it is well-settled law that a disclosure can be "entirely adequate to anticipate a claim to [an invention] . . . and, at the same time, entirely inadequate to support the allowance of such a claim."[90] As a result, new drugs can become unpatentable before anyone ever has a chance to patent them. There are at least three different scenarios in which this situation arises: when researchers publish preliminary research about a drug but do not have enough evidence to demonstrate its therapeutic value; when researchers mistakenly believe a new drug is ineffective and disclose it as such; and when researchers disclose a new drug without recognizing their own discovery.

In the first scenario, which is probably the most common of the three, a drug becomes unpatentable because the researchers who first disclosed it did not have the evidence needed to demonstrate its medicinal value to patent it. Patents only cover inventions that are "useful,"[91] and drug patents must contain "more than respectable guesses as to the likelihood of [the drug's] success."[92] Although the Patent and Trademark Office ("PTO") does not require clinical-trial data,[93] it usually demands evidence from laboratory or animal experiments to substantiate the asserted therapeutic

[90] In re Hafner, 410 F.2d 1403, 1405 (C.C.P.A. 1969); *see also* In re Samour, 571 F.2d 559, 563-64 (C.C.P.A. 1978); In re Schoenwald, 964 F.2d 1122, 1123-24 (Fed. Cir. 1992).
[91] 35 U.S.C. § 101.
[92] Rasmusson v. SmithKline Beecham Corp., 413 F.3d 1318, 1325 (Fed. Cir. 2005); *see also* Brenner v. Manson, 383 U.S. 519, 536 (1966). The statutory foundation for this requirement lies in the utility and enablement standards of 35 U.S.C. §§ 101, 112. *See* Rasumsson, 413 F.3d at 1323.
[93] *See* In re Brana, 51 F.3d 1560, 1567-68 (Fed. Cir. 1995).

utility of the drug,[94] and often rejects drug patents for failing to meet this standard.[95] While the disclosure of a new drug without adequate preclinical evidence is not enough to support a patent,[96] such a disclosure can still anticipate a subsequently-filed patent on the drug[97] – even if that disclosure was an earlier patent application rejected by the PTO for lack of utility.[98] In the Ultracet® case, the initial disclosure merely speculated about the drug's effects, and offered no evidence that it would actually work.[99] There are at least four other analogous cases, involving an anti-inflammatory drug,[100] a treatment for

[94] *See* In re Fisher, 421 F.3d 1365, 1377 (Fed. Cir. 2005); U.S. PATENT & TRADEMARK OFFICE, MANUAL OF PATENT EXAMINING PROCEDURE § 2107.03 (8th ed. 2001); JOHN R. THOMAS, PHARMACEUTICAL PATENT LAW 57-83 (2005).
[95] *See* BECKER, *supra* note 56, at § 6.31.
[96] In re Fisher, 421 F.3d at 1377-78.
[97] *See, e.g.*, In re Hafner, 410 F.2d 1403, 1405 (C.C.P.A. 1969) (invalidating a patent on artificial resins).
[98] The combination of the novelty and utility requirements can create a significant barrier to patenting drugs for diseases that are currently difficult to treat. Patent applications are typically published 18 months after being filed. 35 U.S.C. § 122(b). Once published, they are considered a printed publication and can anticipate other patents, regardless of whether the PTO rejected the application for lack of utility. *See* 35 U.S.C. § 102(e). If a different set of researchers later try to patent the drug, their claim will likely be anticipated by the prior application. *Id*. The researchers who submitted the original patent application can submit another one that includes sufficient evidence of utility, but only if they are able to do so within 12 months of when their original patent application was published. *See id*. at § 102(b). The PTO usually requires evidence of efficacy from laboratory or animal models for the targeted condition that are known to correlate with efficacy in humans, and if scientists have not yet had any success in treating the disease, these models are difficult to verify. *See* Iver P. Cooper, *Training Materials for Examining Patent Applications with Respect to 35 U.S.C. Section 112, First Paragraph – Enablement Chemical/Biotechnical Applications*, 3 BIOTECHNOLOGY & LAW APPENDIX H15, exs. K, L (2006); *In re Balzarini*, 1991 WL 332576, at *3-7 (Bd. Pat. App. & Interf. Mar. 21, 1991). Consequently, even this 30-month timeframe can be a problem for drugs that target conditions which are poorly understood or are resistant to treatment. *See, e.g.*, Rasmusson v. SmithKline Beecham Corp., 413 F.3d 1318, 1327 (Fed. Cir. 2005); In re MacLeod, 2003 WL 25277951, at *3-9 (Bd. Pat. App. & Interf. Sept. 4, 2003).
[99] Ortho-McNeil Pharm. Inc. v. Caraco Pharm. Labs. LTD., No. 04-CV-73698, 2005 WL 2679788, at *1 (E.D. Mich. Oct. 19, 2005) (discussing the patent disclosure that invalidated most of the claims in the Ultracet® patent). The 1972 disclosure did not contain evidence of the synergistic benefit of combining tramadol and acetaminophen, *see* U.S. Patent 3,652,589, at 12, which was critical for its patentability. *Cf.* Merck & Co., Inc. v. Biocraft Labs., Inc., 874 F.2d 804, 808-09 (Fed. Cir. 1989).
[100] In *SmithKline Beecham Corp. v. Copley Pharmaceutical, Inc.*, the Federal Circuit held that a patent on nabumetone (Relafen®), an anti-inflammatory drug, was invalidated by an earlier publication that merely disclosed the chemical structure of the compound, without any mention of its possible medicinal uses. 45 Fed. Appx. 915, 916-17 (Fed. Cir. 2002); *see also* In re '639 Patent Litig., 154 F. Supp. 2d at 162. Although SmithKline Beecham held a separate patent on Relafen®'s medical use that was not anticipated by the prior disclosure, that patent expired less than three years after the FDA first approved the drug, much earlier than the patent on Relafen® itself. *See* In re '639 Patent Litig., 154 F. Supp. 2d at 159, 166 n.8.

prostate cancer,[101] a drug for hypertension and angina,[102] and an osteoporosis treatment.[103] In each of these cases, the courts invalidated a drug patent based on a publication that failed to provide an adequate disclosure of the drug with its claimed utility.[104] Whenever researchers disclose a drug without establishing its therapeutic value, therefore, they can potentially undermine the novelty of the drug, rendering it unpatentable.

The second scenario in which valuable new drugs sometimes enter the public domain prematurely is when they initially appear to be ineffective in early experiments. On at least two separate occasions the courts invalidated patents claiming what later became a FDA-approved use for a drug – a chemotherapy treatment[105] and a treatment

---

[101] In *Rasmusson v. SmithKline Beecham Corp.*, the Federal Circuit invalidated several patents on the use of finasteride (Proscar®) to treat prostate cancer, finding them to be anticipated by a previous, unsuccessful attempt to patent the same treatment, even though that earlier attempt "fail[ed] to provide any data to demonstrate the effects of finasteride in treating prostate cancer." 413 F.3d 1318, 1322, 23-27 (Fed. Cir. 2005). At the time of this decision, finasteride was already on the market as a treatment for benign prostatic hyperplasia and male-pattern baldness. The drug's role as a treatment for prostate cancer is remains experimental. *See* Robert L. Leibowitz & Steven J. Tucker, *Treatment of Localized Prostate Cancer with Intermittent Triple Androgen Blockade: Preliminary Results in 110 Consecutive Patients*, 6 ONCOLOGIST 177 (2001); William K. Oh et al., *Finasteride and Flutamide Therapy in Patients with Advanced Prostate Cancer: Response to Subsequent Castration and Long-Term Follow-Up*, 62 UROLOGY 99 (2003).

[102] In *In re Metoprolol Succinate Patent Litig.*, __ F.3d __ (Fed. Cir. 2007), the Federal Circuit invalidated the patent on metoprolol succinate (Toprol-XL®), a controlled-release drug for hypertension and angina, based on an earlier patent filed by the patentee that claimed a specific formulation of the drug, *id*. at _, even though the older patent was too narrow to effectively block generic competition.

[103] In *Merck & Co. v. Teva Pharms. USA, Inc.*, 395 F.3d 1364 (Fed. Cir. 2005), the Federal Circuit invalidated a patent on the once-weekly dosage of Fosamax®, an osteoporosis drug, based on an article in an industry newsletter that suggested a similar dosing schedule. *Id*. at 1373-77 (invalidating the patent on grounds of obviousness, rather than anticipation, because the article recommended a slightly different dosage). Although the article that invalidated the patent was not peer-reviewed, presented no evidence on the safety or efficacy of using Fosamax® once weekly, and its author had no formal training in pharmacology or medicine, *see* Merck & Co., Inc. v. Teva Pharms. USA, Inc., 288 F. Supp. 2d 601, 618 & n.1, 629 (D. Del. 2003), the Federal Circuit found that "Merck's idea added nothing to what came before," and that there is no reason "why Merck and not [the author of the article] should get credit for the idea." 395 F.3d at 1375. The court did not mention that the author never patented the idea.

[104] *See supra* notes 100-102.

[105] The decision in *Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc.*, 246 F.3d 1368 (Fed. Cir. 2001), involved two patents on a method of reducing blood toxicity during chemotherapy by administering paclitaxel (Taxol®) over a three-hour period. *Id*. at 1371-72, 77-81. Although physicians initially administered Taxol® over a 24-hour period, that practice changed after the release of the clinical-trial data demonstrating the safety and efficacy of a 3-hour administration period. *See* C. Williams et al., *Shorter*

for peptic ulcers[106] – based on publications that discussed the (subsequently) patented use for the drug, but described it as being ineffective.[107] These decisions reflect the courts' highly formalistic approach to the novelty requirement, wherein "[a] reference is no less anticipatory if, after disclosing the invention, the reference then disparages it."[108] As a result of this rule, the novelty requirement prevents the patenting of medical treatments that were initially thought to be ineffective, even when it later appears that those treatments work and would be valuable if proven safe and effective in clinical trials.

The third situation in which this problem arises is when researchers disclose a new drug to the public without realizing what they discovered, thereby failing to patent the new drug while simultaneously making it impossible for anyone else to patent it. While this scenario may sound farfetched, in 2005 and 2006 alone the Federal Circuit invalidated three pharmaceutical patents – covering an inhalation anesthetic,[109] an

---

Verses Longer Duration of Infusion of Paclitaxel for any Advanced Adenocarcinoma (Review), THE COCHRANE LIBRARY 2007, Issue 2, at 2-4, 7-8. A generic version of Taxol® was already on the market when the Federal Circuit invalidated Bristol-Myers Squibb's patent, and thus it is unclear whether the decision had any financial repercussions for the patentee. *See* Jennifer E. Smith, *Generic Taxol Gets Production Boost*, DRUG STORE NEWS, Jul. 23, 2001, at 16.

[106] The decision in *Astra Akteibolag v. Andrx Pharms., Inc.*, 222 F. Supp. 2d 423 (S.D.N.Y. 2002) related to several patents on the use of omeprazole (Prilosec®), including a patent on the use of that drug in the treatment of ulcers. *Id*. at 591-98. The use of Prilosec® along with antibiotics now plays an important role in the treatment of peptic ulcers, *see* NIH Consensus Development Panel on Helicobacter pylori in Peptic Ulcer Disease, *Helicobacter Pylori in Peptic Ulcer Disease*, 272 J AM. MED. ASS'N 65, 67-68 (1994), although it took a long time for the medical community to embrace this treatment. *See* Barry J. Marshall, *The Discovery that Helicobacter Pylori, a Spiral Bacterium, Caused Peptic Ulcer Disease*, *in* HELICOBACTER PIONEERS: FIRSTHAND ACCOUNTS FROM THE SCIENTISTS WHO DISCOVERED HELICOBACTERS: 1892-1982, at 199-201 (Barry Marshall ed., 2002). For a discussion of the debate among physicians over the use of acid-blocking drugs and antibiotics in the treatment of peptic ulcers, and the intellectual property issues that affected that debate, *see infra* note 321.

[107] *See* Bristol-Myers Squibb, 246 F.3d at 1377-81; Astra Akteibolag, 222 F. Supp. 2d at 596-98.

[108] Bristol-Myers Squibb, 246 F.3d at 1378 (*quoting* Celeritas Techs. Ltd. v. Rockwell Int'l Corp., 150 F.3d 1354, 1361 (Fed. Cir. 1998)).

[109] In *Abbott Laboratories v. Baxter Pharmaceutical Products, Inc.*, the Federal Circuit invalidated a patent on the mixture of water and sevoflurane (a "fast-acting, highly effective inhalation anesthetic"), a combination that prevents the sevoflurane from degrading and becoming toxic during transport and storage. 471 F.3d 1363, 1365 (Fed. Cir. 2006). The Court held that the patent was inherently anticipated by an older patent covering a process of purifying sevoflurane, which involved adding water and then distilling away all the water and other impurities. *Id*. at 1369. Although "knowledge of the beneficial nature of a water-sevoflurane mix was wholly lacking" before the patentee discovered that water prevented

antidepressant,[110] and a drug used to assess calcium metabolism and bone health[111] – under these exact circumstances. In each of the three cases, not only was the public not using the product before the patentee rediscovered and developed it for medical use, but prior to the patentee's efforts, no one even knew the product existed.[112] Under the doctrine of inherent anticipation, however, the disclosure of a drug in some unrecognizable form is still sufficient to invalidate a later-filed patent on that drug, since the prior "lack of knowledge [about the drug] is wholly irrelevant to the question of whether the . . . patent claims something 'new' over the [earlier] disclosure."[113]

---

sevoflurane from becoming toxic while in storage, the court explained "that a reference may anticipate even when the relevant properties of the thing disclosed were not appreciated at the time." *Id*. at 1367. The original patent on sevoflurane expired before the drug was approved by the FDA. *See Abbott Labs. v. Baxter Pharm. Prods., Inc.*, No. 01 C 1867, 2005 WL 2347221, at *1 (N.D. Ill. Sept. 22, 2005).

[110] In *SmithKline Beecham Corp. v. Apotex Corp.*, the Federal Circuit invalidated a patent on the antidepressant drug paroxetine hydrochloride (Paxil®) on the ground that it had previously been produced in trace, undetected amounts during the process of manufacturing an older experimental version of the drug. 403 F.3d 1331, 1343-45 (Fed. Cir. 2005). The Court acknowledged that the newer version of Paxil® "was not even discovered until years after" the older version was first manufactured, but explained that "inherent anticipation does not require [that anyone have] . . . recognize[d] the inherent disclosure in the prior art at the time the prior art is created." *Id*. at 1343. The patent on the older version expired before the FDA ever approved the drug, and the patent on the newer version was not set to expire until 2006. *See* SmithKline Beecham Corp. v. Apotex Corp., 247 F. Supp. 2d 1011, ___, 1017 (N.D. Ill. 2003), *aff'd on other grounds*, 403 F.3d 1331 (Fed. Cir. 2005). The first generic version of Paxil® entered the U.S. market in September 2003. *See* Press Release, Apotex Corp., *Apotex Launches First Generic Version of Paxil®*, Sept. 8, 2003, *at* http://www.apotexcorp.com/press/GenericPaxil09082003.htm.

[111] In *Nichols Institute Diagnostics, Inc. v. Scantibodies Clinical Laboratory, Inc.*, the Federal Circuit held that a patent on certain antibodies – used to measure the blood levels of Human Parathyroid Hormone ("Human PTH") – was anticipated by one of the inventors' own abstracts, in which they had unwittingly disclosed the patented antibodies. 195 Fed. Appx. 947, 948-49, 51-52 (Fed. Cir. 2006). The abstract disclosed ten separate blood serums, each containing a mixture of antibodies that, according to the abstract, "provided the possibility to specifically detect . . . human PTH." *Id*. at 948. Although "the significance of the claimed antibody was not known until after the abstract was submitted," the Court still held that the patent was inherently anticipated by the abstract. *Id*. at 952.

[112] Abbott Labs., 471 F.3d at 1367; SmithKline Beecham, 403 F.3d at 1343; Nichols Inst. Diagnostics, 195 Fed. Appx. at 948-49.

[113] Abbott Labs., 471 F.3d at 1368. Dan Burk and Mark Lemley, who defend the inherent-anticipation doctrine, describe it as a "categorical judgment that an invention already being used by the public shouldn't be patentable because someone discovers information about how it works." Dan L. Burk & Mark A. Lemley, *Inherency*, 47 WM. & MARY L. REV. 371, 383-84 (2005); *cf.* MERGES & DUFFY, *supra* note 65, at 388-89. There are two problems with this argument. First, recent opinions from the Federal Circuit – including the ones discussed above – establish that an invention is inherently anticipated if it merely existed in prior literature or practice, regardless of whether anyone has previously benefited from it. *See supra* text accompanying note 112. Second, Burk and Lemley incorrectly assume that "in cases in which the public is already benefiting from the invention, the additional value of learning exactly how or why they benefit does

Consequently, whenever a drug is unknowingly disclosed to the public, it can cease to be novel before anyone knows about it, and the patent system will no longer reward any efforts to discover it or establish its therapeutic value.

As strange as these three rules might sound, they have been relatively uncontroversial among most patent-law scholars.[114] Indeed, it is sometimes thought that an expansive novelty requirement is needed to prevent pharmaceutical companies from abusing the patent system by continually filing new patents on old drugs to delay entry by generic competitors, a practice known as "evergreening."[115] The courts could use other doctrines to more precisely target and block these abusive strategies, however, such as an equitable defense to infringement for generic manufacturers.[116] The novelty doctrine may prevent some evergreening,[117] but it can also prevent researchers from patenting therapeutically valuable drugs that have not yet been developed, as seen with many of the drugs mentioned above.[118] The rule is designed to prohibit researchers from patenting any drug that was previously used or described in a publication, regardless of whether the earlier disclosure allowed the public to benefit from the drug's use, or even whether it would have allowed the inventor to patent the drug. Under the novelty requirement,

---

not seem worth withdrawing from the public the use of an invention that they already enjoy." Burk & Lemley, *supra*, at 383. While this may be true for some inventions, it is not for others; the value of pharmaceutical innovation, for example, depends heavily on the production of information about whether a drug is safe and effective. *See* JERRY AVORN, POWERFUL MEDICINES: THE BENEFITS, RISKS, AND COSTS OF PRESCRIPTION DRUGS 39-68 (2005).

[114] *See, e.g.*, MERGES & DUFFY, *supra* note 65, at 388-89.

[115] *See* Natalie M. Derzko, *The Impact of Recent Reforms of the Hatch-Waxman Scheme on Orange Book Strategic Behavior and Pharmaceutical Innovation*, 45 IDEA 165, 186-87, 220-21 (2005); *cf.* Rebecca S. Eisenberg, *The Role of the FDA in Innovation Policy*, 13 MICH. TELECOMM. & TECH. L. REV. 345, 354 & n.37 (2007). The phenomenon of evergreening dates back to at least the 1930s. *See* MACHLUP, PATENT SUBCOMM. REPORT, *supra* note 12, at 10 & n.50.

[116] *See* SmithKline Beecham Corp. v. Apotex Corp., 247 F. Supp. 2d 1011, 1043-52 (N.D. Ill. 2003) (Posner, J.), *aff'd on other grounds*, 403 F.3d 1331 (Fed. Cir. 2005).

[117] Some of the drugs mentioned above were possibly the subject of abusive patent litigation by pharmaceutical companies, including the cases involving Prilosec®, Taxol® and Paxil®, discussed at *supra* notes 105, 106 & 110.

[118] *See supra* notes 99-102, 109, 111.

therefore, negligible disclosures can – and have – prevented socially valuable drugs from being patented.

3. Falling into the Novelty Trap

Given the current structure of the novelty requirement, it is not uncommon for new drugs to be disclosed prematurely such that later they cannot be patented. The hair-trigger approach to the novelty requirement discussed above is particularly problematic for the drugs discovered at universities, where researchers are rewarded more for publishing their research results than for patenting them, and are thus prone to disclosing a new drug before securing patent rights over it. This same problem occurs in private industry, although under different circumstances. Pharmaceutical companies often disclose drugs prematurely by filing broad patent applications that cover many more drugs than they plan to develop, and subsequently discard most of those drugs into the public domain. The regularity with which potential drugs are disclosed under these circumstances suggests that Ultracet® is not an isolated occurrence, and that there are likely many other drugs that lose their novelty before the public gains access to them. The large number of PTO decisions rejecting drug-patent applications for lack of novelty is consistent with this conclusion.

Novelty is often a barrier to the patenting of drugs discovered in university laboratories. Academic researchers are frequently the first to identify new drugs,[119] and

[119] Of the new drugs approved by the FDA between 1998 and 2003, at least 15% were originally identified through publicly-funded research. *See* Robert Kneller, *The Origins of New Drugs*, 23 NATURE BIOTECHNOLOGY 529, 529-30 (2005).

publishing is an important part of their work.[120] Although many academics try to keep their inventions secret before filing a patent application,[121] it is not always clear what information must be withheld to preserve the novelty of an invention,[122] and the pressure to publish makes it difficult for them to keep their research secret for any extended period of time.[123] As a result, it is not uncommon for university inventions to be disclosed to the public more than one year before anyone tries to patent them.[124] According to a recent survey of universities with large medical-research programs, 82% were unable to patent at least one of their life-science inventions during the previous year "because research outcomes were already published," and 71% were unable to find a commercial partner to develop one or more of their life-science inventions for the same reason.[125] These survey

[120] *See* Richard Monastersky, *The Number That's Devouring Science: the Impact Factor, Once a Simple Way to Rank Scientific Journals, has Become an Unyielding Yardstick for Hiring, Tenure, and Grants*, CHRONICLE OF HIGHER EDUCATION, Oct. 14, 2005, at A12.

[121] *See* Eric C. Campbell & Eran Bendavid, *Data-Sharing and Data-Withholding in Generics and the Life Sciences: Results of a National Survey of Technology Transfer Officers*, 6 J. HEALTH CARE L. & POL'Y 241, 250-51 (2003); Jeremy M. Grushcow, *Measuring Secrecy: A Cost of the Patent System Revealed*, 33 J. LEGAL STUD. 59, 63-67, 69-75 (2004).

[122] *See, e.g.*, Nichols Institute Diagnostics, Inc. v. Scantibodies Clinical Laboratory, Inc., 195 Fed. Appx. 947, 948-49, 51-52 (Fed. Cir. 2006).

[123] *See* Joshua A. Newberg & Richard L. Dunn, *Keeping Secrets in the Campus Lab: Law, Values and Rules of Engagement for Industry-University R&D Partnerships*, 39 AM. BUS. L.J. 187, 207-09 (2002).

[124] *Cf.* Loius P. Berneman & Kathleen A. Denis, *University Licensing Trends and Intellectual Capital*, *in* BIOTECHNOLOGY LAW 2002: BIOTECHNOLOGY PATENTS & BUSINESS STRATEGIES, at 565 (PLI Pats., Copyrights, Trademarks, and Literary Prop. Course, Handbook Series No. G0-0129, 2002), WL 718 PLI/Pat 551 (noting that it is often very difficult for universities to file timely patent applications on their employees' inventions).

[125] *See* Campbell & Bendavid, *supra* note 121, at 250-53. Some of these life-science inventions are likely to be new drugs, *cf.* Mark G. Edwards et al., *Value Creation and Sharing Among Universities, Biotechnology and Pharma*, 21 NATURE BIOTECHNOLOGY 618 (2003), while others are probably research tools used to discover new drugs. *See* Annetine C. Gelijns & Samuel O. Thier, *Medical Innovation and Institutional Interdependence: Rethinking University-Industry Connections*, 287 J. AM. MED. ASS'N. 72, 73-74 (2002). Some, but not all, of the life-science research tools developed at universities need a patent to be developed. *See* Arti K. Rai & Rebecca S. Eisenberg, *Bayh-Dole Reform and the Progress of Biomedicine*, 66 SPG LAW & CONTEMP. PROBS. 289, 302-03 (2003); Jeannette Colyvas et al., *How Do University Inventions Get Into Practice*, 48 MGMT. SCI. 61, 65 (2002).

results are consistent with anecdotal evidence that universities sometimes fail or are unable to patent their faculty members' inventions,[126] including new drugs.[127]

This problem extends beyond the drugs discovered at universities, however, as pharmaceutical companies themselves regularly disclose drugs in a manner that later prevents them from being patented. Although researchers in the private sector occasionally publish without realizing that they are undermining the novelty of their invention,[128] these types of mistakes are more common at universities.[129] When pharmaceutical companies disclose drugs prematurely, it is often while they are prosecuting their patents before the PTO. Pharmaceutical companies file their drug patents during early R&D, when they are still trying to select a lead compound from

---

[126] *See, e.g.*, Paul Citron, *Research Interactions Between Industry and Academia: A Corporate Perspective*, 39 THE PHYSIOLOGIST 81, 91-92 (1996); Lorelei Ritchie de Larena, *The Price of Progress: Are Universities Adding to the Cost?*, 43 HOUS. L. REV. 1373, 1380-81 (2007); Owen-Smith & Powell, *supra* note 41, at 109-10; Jerry G. Thursby & Marie C. Thursby, *Who Is Selling the Ivory Tower? Sources of Growth in University Licensing*, 48 MGMT. SCI. 90, 93 (2002). One reason why universities are unable to patent all of their important drug-related discoveries is that faculty members sometimes fail to inform the universities of their inventions in a timely manner. *See, e.g.*, Owen-Smith & Powell, *supra* note 41, at 109-10; Thursby & Thursby, *supra*, at 93. Another reason is that universities have limited resources available to fund their patenting offices, *see* Owen-Smith & Powell, *supra* note 41, at 99, 102-03; Jerry G. Thursby et al., *Objectives, Characteristics and Outcomes of University Licensing: A Survey of Major U.S. Universities*, 26 J. TECH. TRANSFER 59, 66 (2001), and therefore file patent applications on only a portion – usually about 50-60% – of the inventions disclosed to them by university employees. *See* Association of University Technology Managers, AUTM U.S. LICENSING SURVEY: FY2005 29-31, *at* http://www.autm.net/pdfs/AUTM_LS_05_US.pdf. Although universities try to patent the inventions most likely to prove commercially viable, their sorting process is necessarily imperfect, and important drug-related discoveries can be left unpatented because they seemed too speculative or the commercial possibilities too remote. *See* Margo A. Bagley, *Academic Discourse and Proprietary Rights: Putting Patents in Their Proper Place*, 47 B.C.L. REV. 217, 263-64 (2006); *NIH: Moving Research from the Bench to the Bedside, Hearing Before the Subcommittee on Health of the House Committee on Energy and Commerce*, 108th Cong. 53 (2003) (prepared statement of Andrew Neighbour, Associate Vice Chancellor for Research, University of California Los Angeles) (comparing the process of selecting the inventions to patent to the process of "the princess kissing frogs in search of a prince").

[127] *See, e.g.*, In re Application of Weichselbaum, 2006 WL 4494416, at *2 (Com'r Pat., May 3, 2006); In re Behr, 2006 WL 2711012, at *2-5 (Sept. 18, 2006); In re Bergeron, 2004 WL 1646439, at *2-4 (Bd. Pat. App. & Interf. 2004).

[128] *See* Maria Souleau, *Legal Aspects of Patent Protection – What A Medicinal Chemist Should Know About Patent Protection*, *in* THE PRACTICE OF MEDICINAL CHEMISTRY 720 (Camille Georges Wermuth ed., 2d. 2003).

[129] *Cf.* Policy Statement, GlaxoSmithKline, Disclosure of Clinical Trial Information (Jan. 2007), *at* http://www.gsk.com/responsibility/downloads/GSK-Public-Policy-on-Disclosure-of-Clinical-Trial-Information.pdf (explaining that pharmaceutical companies screen their employees' publications before publication to prevent premature disclosures).

numerous potential drugs with similar yet distinct properties.[130] Not knowing which compound they will end up developing, the pharmaceutical companies draft their initial patent application broadly to disclose, and hence establish priority over, as many of the compounds under consideration as possible.[131] As their research progresses, and the companies decide upon a compound to develop, they narrow their patent claims and allow many of the originally disclosed drugs to fall into the public domain.[132] Although these discarded drugs could prove valuable in subsequent research,[133] their prior disclosure will likely defeat any later claim of novelty, thus preventing them from being patented.

An analogous problem arises with the drugs that pharmaceutical companies patent but later abandon before completing their development. Pharmaceutical companies usually investigate thousands of compounds before finding one that they are willing to take into clinical trials.[134] Although firms try hard to identify and develop the drugs that will prove safe and effective (and profitable), their selection process is far from perfect.[135] Subsequent scientific developments might make a drug look promising that was previously abandoned by private industry due to perceived lack of therapeutic value.

---

[130] *See* Bruno Galli & Bernard Faller, *Discover a Drug Substance, Formulate and Develop it to a Product*, *supra* note 128, at 688; Stephen T. Schreiner & Patrick A. Doody, *Patent Continuation Applications: How the PTO's Proposed New Rules Undermine an Important Part of the U.S. Patent System with Hundreds of Years of History*, 88 J. PAT. & TRADEMARK OFF. SOC'Y 556, 557 (2006); Souleau, *supra* note 128, at 721.

[131] *See* Association of the British Pharmaceutical Industry, *Response to the Gowers Review of Intellectual Property Call for Evidence* 4; GRAHAM PATRICK, MEDICINAL CHEMISTRY 177-78 (2001); Schreiner & Doody , *supra* note 130, at 557; Souleau, *supra* note 128, at 721.

[132] *See* Schreiner & Doody , *supra* note 130, at 557. Cf. PHILIP W. GRUBB, PATENTS FOR CHEMICALS, PHARMACEUTICALS AND BIOTECHNOLOGY: FUNDAMENTALS OF GLOBAL LAW, PRACTICE AND STRATEGY 321 (4th ed. 2004).

[133] *See infra* note __.

[134] *See* Mitscher & Dutta, *supra* note 40, at 108-09.

[135] "Scientists and other professionals in the industry are poor in predicting complex responses to drugs . . . . As a direct result, drug development remains part science and part art." TAMAS BARTFAI & GRAHAM V. LEES, DRUG DISCOVERY: FROM BEDSIDE TO WALL STREET 258 (2006); *see also* Pedro Cuatrecasas, *Drug Discovery in Jeopardy*, 116 J. CLINICAL INVESTIGATIONS 2837 (2006).

Moreover, given the unpredictability of drug development, company scientists can easily misjudge the therapeutic potential of a drug, selecting a compound for development that dead-ends while ignoring others that would have proven effective if tested.[136] Corporate executives can make similar errors, dropping a drug from their company's pipeline due to a mistaken judgment about its therapeutic value or market potential.[137] By the time these drugs are discarded, many have already been patented, and the clock on their patent life is running down. Even if another company believed that the drug might be valuable, the diminishing window of potential market exclusivity over the drug usually deters licensing.[138] When pharmaceutical companies drop a drug from their pipeline, therefore, most stop paying the upkeep fees on the patent, hastening the drug's entrance into the public domain.[139]

Although it is impossible to know exactly how many drugs fall into the public domain under these circumstances, the number appears to be large. One sign of the problem is that the PTO has rejected numerous pharmaceutical patents for lack of

---

[136] *See* Ralph Hirschmann, *Introduction*, *in* 11 PHARMACEUTICAL BIOTECHNOLOGY: INTEGRATION OF PHARMACEUTICAL DISCOVERY AND DEVELOPMENT: CASE HISTORIES 2-3 (Ronald T. Borchardt et al. eds. 1998).

[137] *See* Cuatrecasas, *supra* note 135, at 2837-39; Graham A. Showell & John S. Mills, *Chemistry Challenges in Lead Optimization: Silicon Isosteres in Drug Discovery*, 8 DRUG DISCOVERY TODAY 551 (2003). There are a number of reasons why a therapeutically valuable drug might be mistaken for one not worth developing and dropped from a company's pipeline, including errors in estimating the costs of clinical trials or likelihood of success, miscalculation of potential market size, poor patient compliance or incorrect dosing during clinical trials, inadequate patient recruitment in clinical trials, and inadequate trial size. *See* BARTFAI & LEES, *supra* note 135, at 43, 57-58, 59-60, 133-34, 158-59. Therapeutically valuable drugs can also be dropped from a company's pipeline for reasons related to internal company politics. *Id*. at 58.

[138] *See* Telephone Interview with Theodore J. Torphy, Ph.D., Corporate Vice President of Science and Technology, Johnson & Johnson, New Brunswick, New Jersey (Feb. 2, 2007) (on file with author) (explaining that competing pharmaceutical companies rarely license compounds from one another during early development). Occasionally an executive or R&D manager at a pharmaceutical company will negotiate with her employer to leave the firm and license one of its "failed" drugs from the employer to develop it. *See* BARTFAI & LEES, *supra* note 135, at 59. Licensing is more practical under these circumstances because the departing executive is aware of the company's earlier research on the drug and, unlike an outside company, would not have to start the entire research project over again.

[139] *See* AstraZeneca, *Gowers Review of Intellectual Property – Call for Evidence*, Apr. 26, 2006, at 5; Kimberly A. Moore, *Worthless Patents*, 20 BERKELEY TECH. L.J. 1521, 1540-41 (2005).

novelty,[140] including ones on drugs for HIV,[141] lung cancer,[142] high cholesterol,[143] strokes,[144] diabetes,[145] malaria[146] and diarrhea.[147] The large number of such decisions is consistent with the other evidence discussed above, including reports from universities that they are frequently unable to patent their life-science inventions due to early disclosures, and the widespread practice among pharmaceutical companies of disclosing more drugs in their patent applications than they ultimately choose to develop. These drugs are apt to fall through the system unprotected as a result of the novelty requirement.

B. The Non-Obviousness Requirement

Much like the novelty doctrine, the non-obviousness requirement excludes valuable drugs from the patent system by ignoring the development and commercialization costs of inventions. The test for non-obviousness focuses on the level of risk in the research that produced the invention, and does not consider the costs and risks of developing that invention into a marketable product. A new drug with beneficial therapeutic properties is therefore considered obvious if those properties would have been

---

[140] *See supra* note 261.

[141] *See* In re Williams, 2005 WL 4773220, at *4 (Bd. Pat. App. & Interf. Jun. 22, 2005); In re Hofmann, 1999 WL 33548892, at *4-5 (Bd. Pat. App. & Interf. Sept. 14, 1999) (rejecting the claims on a compound proposed as a treatment for HIV, but allowing the method-of-use claims to issue); In re Murrer, 1995 WL 1696811, at *4-6 (Bd. Pat. App. & Interf. 1995); In re Ames, 2007 WL 1033514 (Bd. Pat. App. & Interf. Mar. 28, 2007); In re Bhagwat, 2004 WL 366282, at *4 (Bd. Pat. App. & Interf. Jan. 6, 2004); In re Feldmann, 2003 WL 25281968, at *2-4 (Bd. Pat. App. & Interf. Mar. 21, 2003); In re Saito, 1999 WL 33230062, at *5-6 (Bd. Pat. App. & Interf. Jun. 9, 1999); In re Flowers, 1994 WL 1709509 (Bd. Pat. App. & Interf. Sept. 22, 1994).

[142] *See* In re MacLeod, 2003 WL 25277951, at *7-9 (Bd. Pat. App. & Interf. Sept. 4, 2003) (rejecting the claims on a drug thought to be effective against breast and lung cancer (among other diseases) based on an earlier-filed application from the inventor that was not enabled – although the PTO allowed several method-of-use claims to issue). *Cf.* In re Behr, 2006 WL 2711012, at *2-5 (Bd. Pat. App. & Interf., Sept. 18, 2006).

[143] *See* In re Levin, 2004 WL 1697793, at *2-4 (Bd. Pat. App. & Interf. 2004); In re Picard, 1995 WL 1696846, at *4 (Bd. Pat. App. & Interf. 1995).

[144] *See* In re Bennett, 2004 WL 318775, at *3-5 (Bd. Pat. App. & Interf. Jan. 1, 2004).

[145] *See* In re Sander-Struckmeier, 2005 WL 4773290, at *3-5 (Bd. Pat. App. & Interf. 2005).

[146] *See* In re D'Antonio, 2001 WL 35825743, at *6-10 (Bd. Pat. App. & Interf. July 24, 2001).

[147] *See* In re Bergeron, 2004 WL 1646439, at *2-4 (Bd. Pat. App. & Interf. 2004).

reasonably expected at the time it was invented. Without clinical trials to demonstrate the drug's safety and efficacy, however, it will not receive FDA regulatory approval and be made available for sale in the United States. As a result, the non-obviousness requirement withholds patent protection from the drugs that seem most promising before they have been developed. Advances in the pharmaceutical sciences often exacerbate this problem by making the drug-discovery process more predictable, which makes it harder for researchers to establish the non-obviousness of new drugs. This perverse tendency in the non-obviousness doctrine leaves a significant gap in the scope of patent protection afforded to new drugs, rendering unpatentable many promising new drugs while penalizing scientific progress in drug discovery.

Part one of this section examines the basic test for non-obviousness as it is applied to new drugs, noting how the doctrine ignores the development and commercialization costs in the industry, and how previous scholars have either overlooked or underestimated this flaw in the drug patent regime. Part two of the section explores the results of this mismatch between the non-obviousness requirement and the economics of drug development.

1. The Non-Obviousness Standard for Drugs

Obvious inventions cannot be patented. In the pharmaceutical industry, this rule means that a drug is unpatentable if its relevant properties were reasonably expected at the time of its invention, regardless of whether it has yet to be proven safe and effective in clinical trials. If the idea for a drug is obvious, therefore, the patent system offers no incentive for private industry to invest in securing its regulatory approval.

The purpose of the non-obviousness requirement is to prevent trivial inventions from being patented.[148] Originally crafted by the judiciary, and later codified by Congress,[149] the non-obviousness doctrine provides that inventions cannot be patented if they would have been obvious to other skilled artisans in the pertinent field at the time they were made.[150] When this test is applied correctly,[151] it excludes "the results of ordinary innovation" from patent protection,[152] while rewarding the inventors who undertake highly uncertain research projects that initially seem unlikely to succeed.[153] This test is often described as "the most important of the basic patent requirements,"[154] and the Supreme Court has repeatedly suggested that non-obviousness is a constitutional limitation on the scope of Congress's patent power.[155]

In the context of pharmaceutical patents, the non-obviousness requirement has been designed to stop researchers from patenting drugs that they "[r]eached by means of routine procedures . . . producing only predictable results."[156] Pharmaceutical patents are considered obvious if there was a "reasonable expectation" that the drug "would work for its intended purpose" at the time it was invented, and there is inadequate "[e]vidence of

---

[148] *See* MERGES & DUFFY, *supra* note 65, at 644.
[149] *See* Graham v. John Deere Co., 383 U.S. 1, 11-17 (1966).
[150] Pursuant to 35 U.S.C. § 103(a), "[a] patent may not be obtained . . . if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains."
[151] The ultimate question of obviousness is not a bright-line rule, *see KSR Int'l Co. v. Teleflex Inc.*, __ U.S. __, [11, 15, 17] (2007), and it can be difficult for the courts to apply the test in a predictable manner. *See* Harries v. Air King Products Co., Inc., 183 F.2d 158, 162 (1950) (L. Hand, J.) (observing that the non-obviousness standard is "as fugitive, impalpable, wayward, and vague a phantom as exists in the whole paraphernalia of legal concepts").
[152] KSR Int'l, __ U.S. at [last page].
[153] *See* Merges, *supra* note 12, at 2.
[154] MERGES & DUFFY, *supra* note 65, at 643; *see also* Menell & Scotchmer, *supra* note 10, at __.
[155] *See* KSR Int'l, __ U.S. at [last page]; Bonito Boats, Inc. v. Thunder Craft Boats, Inc., 489 U.S. 141, 146 (1989); Graham v. John Deere Co., 383 U.S. 1, 5-6 (1966).
[156] Merck & Co. v. Biocraft Labs., Inc., 874 F.2d 804, 809 (Fed. Cir. 1989); *see also* Pfizer, Inc. v. Apotex, Inc., 480 F.3d 1348, 1365-69 (Fed. Cir. 2007).

unexpected results" in the drug's performance.[157] Courts apply this test through the eyes of a hypothetical "skilled artisan" in the field,[158] whom they generally define as an experienced drug researcher or medicinal chemist.[159] Unless such a person would have been surprised by the drug's properties and successful test results, it cannot be patented under the non-obviousness standard.

Much like the novelty doctrine, the doctrinal test for non-obviousness ignores the development and commercialization costs of inventions, assuming that once the idea for an invention becomes accessible to the public through its obviousness, the invention itself will also be available.[160] The goal of the non-obviousness requirement is to ensure that the patent system rewards only those inventions that would not have been created absent the inducement of a patent.[161] Since obvious ideas are likely to occur to people even without a patent as a reward, patent protection is thought to be unnecessary.[162] In reality, the public often cannot benefit from a new idea until someone has invested to develop and commercialize it.[163] Nonetheless, these post-invention costs are irrelevant to judicial determinations of obviousness.[164] The non-obviousness standard is therefore based on

---

[157] Pfizer, 480 F.3d at 1368, 70; *see also* Eli Lilly and Co. v. Zenith Goldline Pharms., Inc., 471 F.3d 1369, 1377-78 (2006). To be more precise, a reasonable expectation of success makes the claimed compound prima facie obvious, and the applicant may rebut that presumption of obviousness with evidence of unexpected results. *See* Yamanouchi Pharm. Co. v. Danbury Pharmacal, Inc., 231 F.3d 1339, 1343 (Fed. Cir. 2000); In re Mayne, 104 F.3d 1339, 1343 (Fed. Cir. 1997).

[158] Pfizer, 480 F.3d at 1361; *see also* 35 U.S.C. § 103(a).

[159] *See, e.g.*, Alza Corp. v. Mylan Labs., Inc., 464 F.3d 1286, 1293 (Fed. Cir. 2006); In re Merck, 800 F.2d at 1096; Pfizer Inc. v. Teva Pharms. USA, Inc., 482 F. Supp. 2d 390, 422-23 (D.N.J. 2007); Janssen Pharmaceutica N.V. v. Mylan Pharms., Inc., 456 F. Supp. 2d 644, 653-54 (D.N.J. 2006); Takeda Chem. Indus., Ltd. v. Mylan Labs., Inc., 417 F. Supp. 2d 341, 373 (S.D.N.Y. 2006).

[160] *See* Robert P. Merges, *As Many As Six Impossible Patents Before Breakfast: Property Rights for Business Concepts and Patent System Reform*, 14 BERKELEY TECH. L.J. 577, 592 n.41 (1999).

[161] *See Graham*, 383 U.S. at 11; *see also* Edmund W. Kitch, Graham v. John Deere Co.*: New Standards for Patents*, 1966 SUP. CT. REV. 293, 301 (1966).

[162] *See* Rebecca S. Eisenberg, *Obvious To Whom? Evaluating Inventions from the Perspective of PHOSITA*, 19 BERKELEY TECH. L.J. 885, 886 (2004); MERGES & DUFFY, *supra* note 65, at 646.

[163] *See supra* note and text accompanying note 13.

[164] *See* Graham v. John Deere Co., 383 U.S. 1, 17-18 (1966) (outlining the basic non-obviousness test).

the dubious assumption that obvious inventions do not have significant development costs, or that firms will always be willing to incur those costs without having a patent on the invention.

This policy of ignoring post-invention costs is particularly troubling in the pharmaceutical industry, where the non-obviousness requirement results in the denial of patent protection to potentially valuable drugs before they have been developed for public use. Although a new drug is considered obvious if an experienced drug researcher would have reasonably expected it to possess its beneficial properties,[165] that expectation will not satisfy the FDA's regulatory requirements. Without clinical trials to demonstrate the drug's safety and efficacy, it will not be approved by the FDA, and thus will not be made available to the public.[166] The cost of those clinical trials alone – without considering the risk of failure – still run in the hundreds of millions of dollars on average;[167] and even drugs with a reasonable expectation of success at the time they are invented usually face significant uncertainty in clinical trials.[168] Yet the patent system offers no reward for investing in those clinical trials if the drug to be tested is considered obvious under the patent laws.

This policy of ignoring the development and commercialization costs of drugs may seem like a glaring failure in the non-obviousness standard, but it has received little

---

[165] *See supra* text accompanying notes 157-159.

[166] *See supra* note and text accompanying note 77.

[167] If success were guaranteed, the mean out-of-pocket cost for clinical trials on a new drug, including the time-value of money, would be over $250 million. *See* DiMasi et al., *supra* note 22, at 172. A relatively small percentage of new drugs, perhaps 30%, generate sufficient revenues during their initial years on the market to recoup these costs. *Cf.* Henry Grabowski et al., *Returns on Research and Development for 1990s New Drug Introductions*, 20 PHARMACOECONOMICS Supp. 11, 22-23 (2002).

[168] Only about one-fifth of the new drug candidates that begin clinical trials ever complete the process and are approved by the FDA, *see* Joseph A. DiMasi, *Risks in New Drug Development: Approval Success Rates for Investigational Drugs*, 69 CLINICAL PHARMACOLOGY & THERAPEUTICS 297, 298 (2001), and very few drugs are ever guaranteed success in clinical trials. *See* George Lasezkay, *An Overview: Attracting Partners in the Pharmaceutical Industry*, 25 RETINA S104 (2005).

attention from patent-law scholars. Several scholars have criticized the test for non-obviousness on the ground that it overlooks the costs of the inventive process,[169] but fewer have commented on the doctrine's failure to consider the *post-invention* costs and uncertainty of developing and commercializing inventions.[170] At least one scholar, Robert Merges, actually argued against consideration of development and commercialization costs of inventions in the test for non-obviousness,[171] although his brief treatment of the issue glossed over the possibility that an obvious invention might not reach the public without a patent to motivate its development.[172] Dan Burk and Mark Lemley recognized the theoretical point that the non-obviousness requirement should

[169] *See, e.g.*, John H. Barton, *Non-Obviousness*, 43 IDEA 475 (2003); Menell & Scotchmer, *supra* note 10, at __; Merges, *supra* note 12, at 4. This argument was first outlined by Robert Merges, who noted that the non-obviousness requirement can deter research "where initial experimentation is very costly" because it fails to consider risk aversion among inventors. *Id*. at 4. Merges observed that when the expected returns from various research projects are equal, risk-adverse firms will prefer the lower-cost and lower-variance projects because they offer a safer investment. *Id*. at 43-69. He therefore recommended "a modest lowering of the standard . . . for research which is very expensive in the early stages." *Id*. at 69.

[170] *See* Stuart Minor Benjamin & Arti K. Rai, *Who's Afraid of the APA? What the Patent System Can Learn from Administrative Law*, 95 GEO. L.J. 269, 278 (2007); Burk & Lemley, *supra* note 21, at 1678; SHAVELL, *supra* note 10, at 152 n.31. Karen Boyd suggested lowering the non-obviousness standard for biotechnology inventions, arguing that given "the cost and likelihood of commercial success" in biotechnology, a lower standard was appropriate to "give the needed incentive to overcome the risk aversion that is otherwise problematic in the industry." Karen I Boyd, *Nonobviousness and the Biotechnology Industry: A Proposal for a Doctrine of Economic Nonobviousness*, 12 BERKELEY TECH. L.J. 311, 339 (1997). Much like Merges, *see supra* note 12, Boyd does not advocate lowering the non-obviousness standard to account for situations where the development and commercialization costs of an obvious invention are greater than the expected profits from marketing it without patent protection. Instead, she argues that the non-obviousness standard should be adjusted to correct for risk aversion. *See* Boyd, *supra*, at 316-18, 337-41.

[171] Merges defended the non-obviousness doctrine's exclusive focus on "the level of uncertainty facing the inventor just prior to the crucial experiment leading up to the patent," contending that "the intrinsic social value of producing information" about "highly uncertain technical challenges" justifies patent protection, whereas the information produced in the post-invention stages of product development and commercialization "would seem to produce relatively few positive externalities." Merges, *supra* note 12, at 33-34. In other words, he believes that awarding patents on the basis of development and commercialization expenses is unwise because those efforts do not "contribute valuable technical information to the relevant technical community." *Id*. at 34, 65-69.

[172] Although Merges focuses on the potentially smaller spill-over benefits from developing inventions, *see supra* note 171, spill-over benefits are of secondary importance when deciding whether to grant a patent on an "obvious" invention that will not reach the public without such protection because of its development and commercialization costs. *See supra* note and text accompanying note 36. Moreover, the spill-over benefits from commercializing inventions can sometimes be substantial. *Cf.* U.S. CONGRESS OFFICE OF TECHNOLOGY ASSESSMENT, INNOVATION AND COMMERCIALIZATION OF EMERGING TECHNOLOGIES 35 (1995).

account for the costs and uncertainties of post-invention efforts, and even noted that such an adjustment could be important for pharmaceuticals.[173] Like Merges, however, they discounted the risk of valuable inventions being considered obvious,[174] and thus saw little problem with the existing non-obviousness standard for drugs.[175] A few other scholars, including John Barton, Stuart Benjamin and Arti Rai, have recognized that valuable drugs might in fact be obvious, and thus be in danger of never being developed.[176] They described this problem only as it relates to certain new drug technologies, however, and did not extend the observation into a general critique of the non-obviousness requirement as it applies to pharmaceuticals. The patent-law literature generally shows little awareness of how the economic logic underlying the non-obviousness test unravels in the

[173] *See* Burk & Lemley, *supra* note 21, at 1678 ("If patents are to drive innovation in biotechnology, rather than merely invention, . . . courts must take account of the cost and uncertainty of post-invention testing and development.").

[174] Reflecting the widely-held assumption that a valuable drug would be patentable, Burk and Lemley make only passing reference to the threat of losing important new drugs due to the non-obviousness requirement. *See* Burk & Lemley, *supra* note 21, at 1681-82 ("Lowering the obviousness threshold makes it more likely that marginal inventions will be patented, but . . . [i]f getting from invention to market is the costly and uncertain part of the endeavor, it is the[] more significant inventions that we need to worry about rewarding.").

[175] To prevent drug companies from designing around the patents on their competitors' successful drugs, Burk and Lemley recommend "a fairly *high* [non]obviousness threshold" for biologic drugs, and perhaps the same for traditional pharmaceuticals as well. Burk & Lemley, *supra* note 21, at 1682, 1684-86. This suggestion follows from their view that the pharmaceutical and biotechnology industries "fit well into [Edmund Kitch's] prospect theory," and thus they advise issuing "[f]ewer and broader patents" in those industries. *Id*. at 1682, 1684-87. Using the non-obviousness standard for this task is problematic, however, because it necessarily creates a zone of unpatentable drugs around each new drug patent or publication, and those unpatentable drugs might have great social value. *See infra* text accompanying notes 184-195. Moreover, it is unclear whether a smaller number of broad patents in pharmaceuticals would be better for promoting innovation. *See infra* note 192.

[176] *See* Barton, *supra* note 169, at 506 ("[T]here is a strong argument that it would be obvious to try particular human proteins as pharmaceuticals, and there would be no investment without the patent system."); Benjamin & Rai, *supra* note 170, at 307-08 (noting that "given the rapid advances of biotechnology, it might be technically obvious to identify a gene that could be used therapeutically," but "without a patent no one would have the incentive to develop the potential therapeutic product"); Philippe Ducor, *New Drug Discovery Technologies and Patents*, 22 RUTGERS COMPUTER & TECH. L.J. 369, 372, 461 (1996) ("[T]he screening of combinatorial molecular libraries by high-throughput receptor assays is potentially powerful enough to render its products (ligands) unpatentable due to obviousness," which "threatens the incentives of the pharmaceutical industry to invest in the ligand's development").

pharmaceutical industry, where any drug (including an obvious one) that is subject to the FDA's rigorous clinical-trial requirements likely needs a patent to incent its development.

2. The Perversity of the Non-Obviousness Requirement as Applied to Drugs

In an industry like pharmaceuticals, where patents are necessary for promoting the development and commercialization of inventions, the non-obviousness requirement performs a pernicious economic function. It denies patent protection to the drugs that appear most likely to succeed at the time they are invented and that have expected beneficial properties; *i.e.*, the drugs that appear most promising in early research. The courts and PTO apply this test without hesitation, finding drugs to be unpatentable whenever their therapeutic properties are considered unsurprising. Although some of these drugs are obvious because their chemical structure is nearly identical to that of existing drugs, which means they may have the same therapeutic effects and be of little value, the patent system is largely incapable of distinguishing these low-value "me too" drugs from important new medicinal agents. In fact, the PTO rejects drug-patent applications for obviousness long before the therapeutic properties of those drugs can be reliably predicted. Moreover, because the non-obviousness test focuses on whether the therapeutic properties of a drug are expected, not whether the drug is socially valuable, the PTO and courts have rejected patent applications on drugs because the drug is expectedly superior to known treatments, and thus is expected to have great social value if developed. This test for non-obviousness is particularly problematic for the efforts of medicinal chemists to create new drugs by enhancing the therapeutic properties of known compounds, since they often enhance those compounds in ways that they reasonably

expect to produce beneficial effects. Ironically, scientific advances in medicinal chemistry actually worsen this problem by making the drug-discovery process more predictable, which generally makes the drugs discovered through those advances more obvious. Given the perversity of these rules, there are likely a great number of drugs that cannot be patented under the non-obviousness requirement; something evidenced by, among other things, the numerous PTO decisions rejecting drug-patent applications on the ground that the claimed invention is obvious.

The most troubling aspect of the non-obviousness requirement is that it denies patent protection to inventions *because* they seemed likely to work while ignoring the question of whether a patent is needed to motivate that invention's development. The non-obviousness doctrine was crafted under the assumption that patents are only necessary for encouraging research that involves significant uncertainty and seems unlikely to produce a working invention.[177] While it is true that the inventions arising out of high-risk research are more likely to require patent protection, since investors might be unwilling to finance that research if competitors could duplicate their successes without taking the same risks, this situation is not the only one where patents are necessary. If the investment required to develop and commercialize an invention is significant and, like the initial research, vulnerable to free-riding imitators, then patent protection becomes increasingly important for the results of both high- and low-risk research projects. Since the standards of non-obviousness ignore these post-invention costs, the rule can discourage investment in the research projects that initially appear to have a high probability of success.

[177] *See* Merges, *supra* note 10, at 2-3, 20-31.

Applying the doctrinal test for non-obviousness to drug patents thus has a perverse effect on the incentives for pharmaceutical innovation, since it withholds patent protection whenever a firm pursues research that appears likely from the start to yield an effective drug. New drugs are considered obvious if an experienced drug researcher would have expected them to possess their beneficial properties at the time they were invented.[178] As a general rule, therefore, the more likely it appears that a new drug will be successful, the less likely it is to be patentable under the non-obviousness requirement.[179] Consequently, the incentive normally provided by patents to invest in the development of new drugs does not exist for the ones that seem most promising in early research.

On some occasions this effect may be rather benign, such as when it denies patent protection to drugs that are so closely related to an older drug that they are unlikely to provide any additional therapeutic benefits. These "me too" drugs, as they are known, are sometimes characterized as worthless inventions that serve only to increase pharmaceutical companies' profits;[180] indeed, some have advocated more vigorous enforcement of the non-obviousness requirement to discourage their development.[181] Under current law, if the similarities between an existing and me-too drug create a reasonable expectation that the me-too drug will succeed in early experiments, then the me-too drug is considered obvious unless it possesses unexpected and superior properties

[178] *See supra* text accompanying notes 157-159.
[179] *See, e.g.*, In re Childers, 2003 WL 25277879, at *4 (Bd. Pat. App. & Interf. Dec. 22, 2003) (rejecting the claims on compounds said to be useful in treating stroke victims because "one of ordinary skill in the art would have reasonably expected the compounds . . . would . . . exhibit the property of binding to the [target] receptor").
[180] *See, e.g.*, MARCIA ANGELL, THE TRUTH ABOUT DRUG COMPANIES: HOW THEY DECEIVE US AND WHAT TO DO ABOUT IT, 74-93 (2005); Peter Lansbury, *An Innovative Drug Industry? Well, No*, WASH. POST, Nov. 16, 2003, at B2.
[181] ANGELL, *supra* note 180, at 80-83; Jerry Avorn, *Sending Pharma Better Signals*, 309 SCI. 669 (2005).

compared to the older drug.[182] The non-obviousness requirement can therefore prevent researchers from patenting a me-too drug that is not genuinely superior to its predecessor. It is unclear whether the public would benefit by not having access to such drugs.[183] Regardless, to the extent that the non-obviousness standards deny patent protection to me-too drugs that provide little or no therapeutic advantage over existing drugs, the doctrine does not pose a catastrophic threat to public welfare.

Unfortunately, the patent system is largely incapable of distinguishing unimportant me-too drugs from drugs of significant medicinal value, and there is little reason to trust that the drugs deemed "obvious" under current law would not provide great benefit to society. By introducing small changes into the chemical structure of an existing drug, scientists sometimes create a superfluous me-too product, but other times produce a new drug with substantially improved therapeutic properties.[184] A new drug that looks similar to an older one can therefore represent a major advance in medical technology.[185] Although these improved versions of known compounds should still be

---

[182] *Compare* Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc., 348 F. Supp. 2d 713, 753-56 (N.D.W. Va. 2004) (upholding the patent on levofloxacin because of its "surprising properties and advantages"), *with* Imperial Chemical Indus., PLC v. Danbury Pharmacal, Inc., 777 F. Supp. 330, 359-65, 369-71 (D. Del. 1991) (invalidating the patent on atenolol due to its "lack of unexpected properties and advantages over the prior art beta-blockers").

[183] *Compare* ANGELL, *supra* note 180, at 80-83 (arguing that me-too drugs have little or no therapeutic value) *with* Albert Wertheimer et al., *Too Many Drugs? The Clinical and Economic Value of Incremental Innovations*, *in* INVESTING IN HEALTH: THE SOCIAL AND ECONOMIC BENEFITS OF HEALTH CARE INNOVATION 77, (79-82) (Irena Farquhar et al., eds., 2005) (arguing that me-too drugs provide patients with valuable choices).

[184] *See* Janos Fischer & Aniko Gere, *Timing of Analog Research in Medicinal Chemistry*, *in* 1 DRUG DISCOVERY AND DEVELOPMENT 199-209 (Mukund S. Chorghade ed. 2006) (providing numerous examples of valuable analogue research in drug development); W. Soudijn, *The Role of Medicinal Chemistry in Drug Research*, 13 PHARMACY WORLD & SCI. 161, 162-65 (1991); Camille G. Wermuth, *Strategies in the Search for New Lead Compounds or Original Working Hypothesis*, *in* THE PRACTICE OF MEDICINAL CHEMISTRY, *supra* note 128, at 71-72 (explaining that me-too drugs are sometimes "as different from the parent molecule as a recent car compared with a forty-year old model").

[185] *See supra* note 184; *cf.* Albert I. Wertheimer et al., *The World Health Organization's Essential Medicines List: An Endorsement of Incremental Innovation and Follow-On Research*, 17 J. PHARMACEUTICAL MARKETING & MGMT. 25 (2007) (finding that 81% of the drugs on the World Health Organization's list of essential medicines are "me too" products).

non-obvious if they have unexpected and superior properties,[186] the PTO is normally required to evaluate the patentability of drugs long before any reliable evidence exists of their possible unexpected benefits.[187] Pharmaceutical patents are typically filed when drugs are in early preclinical research,[188] whereas the important properties of drugs are often not known until later on in preclinical development,[189] and accurate predictions of their therapeutic value are almost always impossible before the completion of clinical trials.[190] Nevertheless, patent examiners are left to judge the therapeutic properties of new drugs based on the results of early preclinical experiments, sometimes rejecting patents on potentially life-saving new drugs because those preclinical-test results were not sufficiently surprising in their judgment.[191] At a point where neither physicians nor the FDA would dare hazard a guess as to the therapeutic effects of a drug, the non-obviousness doctrine requires the PTO to make those judgments. The patent system is

[186] *See supra* note and text accompanying note 157.
[187] *See* MANUAL OF PATENT EXAMINING PROCEDURE, *supra* note 94, at §§ 2141, 2143.02, 2144.09.
[188] *See* Bruno Galli & Bernard Faller, *Discover A Drug Substance, Formulate and Develop It To A Product*, *in* THE PRACTICE OF MEDICINAL CHEMISTRY, *supra* note 128, at 688; Harold C. Wegner & Stephen Maebius, *The Global Biotech Patent Application*, *in* BIOTECHNOLOGY LAW: BIOTECHNOLOGY PATENTS & BUSINESS STRATEGIES IN THE NEW MILLENNIUM, at 129-30 (PLI Pats., Copyrights, Trademarks, and Literary Prop. Course, Handbook Series No. G0-00R6, 2001).
[189] *See* Galli & Faller, *supra* note 188, at 689; Wermuth, *supra* note 184, at 72.
[190] *See* GOVERNMENT ACCOUNTABILITY OFFICE (GAO), U.S. CONGRESS, NEW DRUG DEVELOPMENT: SCIENCE, BUSINESS, REGULATORY, AND INTELLECTUAL PROPERTY ISSUES CITED AS HAMPERING DRUG DEVELOPMENT EFFORTS 25-26 (2006).
[191] *See, e.g.*, In re Cuthbertson, 2007 WL 1766994, at *3-5 (Bd. Pat. App. & Interf. 2007) (rejecting the claims to a cancer-diagnostic agent because there was "no evidentiary support for Appellants' statement that the results obtained with 'present invention' are 'unexpectedly' better and 'superior' when compared to [the older] compounds"); In re Stapleton, 2006 WL 1665384, at *3-6 (Bd. Pat. App. & Interf. 2006) (rejecting a patent on an HIV drug for obviousness because there was insufficient evidence that it "exhibited any unexpected benefit over that taught by the combination of prior art relied upon by the examiner"); In re Bodmer, 2004 WL 77132, at *3-8 (Bd. Pat. App. & Interf. 2004) (rejecting a patent on a drug for pulmonary and other fungal infections on grounds of obviousness because there was "no evidence that the claimed compositions have any unexpected properties compared to the closest prior art"); In re Del Bianco, 1996 WL 1799830, at *1-2 (Bd. Pat. App. & Interf. Jan. 1, 1996) (rejecting the claims to a method of treating breast cancer through the combined administration of two drugs because there was insufficient evidence that the "results are unexpectedly synergistic").

not designed to differentiate between superfluous and important drugs, and an extraordinarily high error rate in these decisions seems inevitable.[192]

Even if the non-obviousness requirement could be administered reliably by the PTO to single out low-value drugs and deny them patent protection, which is doubtful, the current doctrine works in an entirely different manner. The test for non-obviousness does not target the drugs with pharmacological properties that are equivalent to existing drugs on the market; instead, it denies patent protection to the drugs that have *expected* pharmacological properties. That expectation often comes from prior disclosures of compounds that were never developed into an FDA approved drug, and thus are not

[192] Even if the patent system where capable of identifying "me too" drugs that will have virtually identical therapeutic properties to previously patented drugs, it would still be dangerous to use the patent system to deter their development. The me-too phenomenon in pharmaceuticals is largely the result of development races, where competing firms begin developing similar compounds – *i.e.*, drugs in the same therapeutic class – at roughly the same time, and end up launching closely related drugs within a few years of one another. *See* Joseph A. DiMasi & Cherie Paquette, *The Economics of Follow-On Drug Research and Development*, 22 PHARMACOECONOMICS 1, 9-10 & fig.4 (Supp. 2, 2004). The PTO could try to stop these races by denying patent protection to all of the drugs in a class other than the first one (or few) to be patented. To the extent to which these development races lead to wasteful R&D expenditures, preventing them would be beneficial. *See* Rai, *supra* note 35, at 205-06; Scherer, *supra* note 18, at 39-45. Moreover, since me-too drugs reduce prices and steal market share from the breakthrough drug that preceded them, blocking their development would increase the expected return from developing breakthrough products. *See* Frank R. Lichtenberg & Tomas J. Philipson, *The Dual Effects of Intellectual Property Regulations: Within- and Between-Patent Competition in the U.S. Pharmaceuticals Industry*, 45 J.L. & ECON. 643, 646-47 (2002). This strategy is risky, however, since the PTO would usually have to decide which drugs in the class can be patented before any of them have proven successful, and they might pick the wrong ones. *See infra* text accompanying notes 188-190. Drug development is very unpredictable and involves a high rate of failure. *See supra* note 167. The first drug in a class to be patented might fail in development, while a patent application claiming what appears to be a me-too drug could turn out to be the only drug in its class to be successfully developed. Rejecting patent applications on me-too drugs could therefore prevent the public from receiving any drug from that class. The PTO could try to avoid this problem by granting a single patent that covers the entire class of drugs, trusting the patent holder to select the best drugs of the class and make the socially optimal investment in their development. *Cf.* Kitch, *supra* note 14. Granting a broad monopoly at such an early stage in pharmaceutical R&D might stifle innovation, however. *Cf.* Merges & Nelson, *supra* note 15. Given the great uncertainty involved in selecting an appropriate lead compound for development, and the difficulty in modifying that compound's structure to maximize its chances of success in clinical trials, *see* Paul W. Erhardt, *Medicinal Chemistry in the New Millennium: A Glance into the Future*, *in* 1 DRUG DISCOVERY AND DEVELOPMENT 17-102 (Mukund S. Chorghade ed., 2006), allowing multiple firms to tackle these problems may sometimes be required for the production of a single successful drug within a class. *Cf.* Mitscher & Dutta, *supra* note 40, at 108-09; Paul D. Leeson & Brian Springthorpe, *The Influence of Drug-Like Concepts on Decision-Making in Medicinal Chemistry*, 6 NATURE REVIEWS DRUG DISCOVERY 881, 886, 889 (2007).

available for use in medical practice.[193] Moreover, even when the PTO compares drugs to existing treatments, it will deny them patent protection if they possess expectedly *superior* properties.[194] If there is a reasonable expectation that a new drug will be superior to known treatments, or perhaps even an expectation that it will be the only successful treatment for a condition, then that drug is not considered to be the product of true inventiveness, and is therefore obvious. For example, in a case where the court was deciding whether to grant a patent on a pain reliever that, in its own words, appeared to possess "substantially greater analgesic effectiveness than one of the most, if not the most, active analgesic compound of the art," the court rejected the application because it thought the drug's superior properties were unsurprising in light of its chemical structure.[195] Although some obvious drugs may be simple clones of existing treatments, others may represent significant advances in medical technology, and the non-obviousness doctrine pays little attention to the difference.

The rule that drugs must have unexpectedly superior properties to be patented can make it especially difficult to patent the drugs created by enhancing compounds with known therapeutic effects.[196] Pharmaceutical companies employ medicinal chemists to turn a known compound – perhaps an existing drug, a failed drug candidate, or any other public-domain compound with known biologic effects – into a safe and effective drug by altering its structure to improve desirable pharmacological properties while minimizing negative ones.[197] Many of these drugs have proven immensely valuable to society,[198] but

---

[193] *See infra* text accompanying note 220.
[194] *See supra* note 191.
[195] In re Carabateas, 345 F.2d 1013, 1017-18 (C.C.P.A 1965).
[196] *See, e.g.*, Alan Dove, *Redesigner Drugs*, 22 NATURE BIOTECHNOLOGY 953 (2004); Wermuth, *supra* note 184, at 70-72, 77-82.
[197] *See* David J. Carini et al., *The Discovery and Development of Angiotensin II Antagonists*, *in* 11 PHARMACEUTICAL BIOTECHNOLOGY, *supra* note 136, at 29-30; Shayne Cox Gad, *Introduction: Drug*

because medicinal chemists work by altering compounds in ways that they expect to produce positive results,[199] the drugs they invent are vulnerable to the "unexpected results" test of non-obviousness. Indeed, the courts have invalidated numerous drug patents under these circumstances,[200] always in accordance with the principle that "any superior property must be *unexpected* to be considered as evidence of non-obviousness."[201] Strict adherence to the non-obviousness standards of this sort generates

---

Discovery in the 21st Century, *in* DRUG DISCOVERY: HANDBOOK 8 (Shayne Cox Gad, ed., 2005); PATRICK, *supra* note 131, at 75.

[198] *See* Cuatrecasas, *supra* note 135, at 2841; Dove, *supra* note 196, at 953; Soudijn, *supra* note 184, at 162-65.

[199] *See* Camille G. Wermuth, *Medicinal Chemistry: Definition and Objectives, the Three Main Phases of Drug Activity, Drug and Disease Classifications*, *in* THE PRACTICE OF MEDICINAL CHEMISTRY, *supra* note 128, at 34. *See generally* THE PRACTICE OF MEDICINAL CHEMISTRY, *supra* note 128, at 173-600.

[200] Pfizer, Inc. v. Apotex, Inc., 480 F.3d 1348, 1368, 1371 (Fed. Cir. 2007) (invalidating the patent on Norvasc® (amlodipine besylate), a drug for the treatment of hypertension and angina. Norvasc® was designed by medicinal chemists to solve problems related to the stability of a closely related compound (amlodipine maleate) that precluded commercialization. The Federal Circuit found that Norvasc® was obvious because the process that led to it "was 'nothing more than routine' application of a well-known problem-solving strategy"); *see also* Alza Corp. v. Mylan Labs., Inc., 464 F.3d 1286, 1295 (Fed. Cir. 2006) (invalidating the patent on controlled-release oxybutynin (Ditropan XL®), a 24-hour urinary incontinence drug, because 'a person of ordinary skill in the art would . . . have perceived a reasonable likelihood of success" in the controlled-release formulation having therapeutic value); Abbott Labs. v. Andrx Pharms., Inc., 452 F.3d 1331, 1345-47 (Fed. Cir. 2006) (denying a motion for a preliminary injunction against Defendant's sale of a generic version of Biaxin XL, a controlled-release antibiotic, because its beneficts in "the reduction of systemic side effects would not be surprising and would not be unexpected"); Merck & Co, Inc. v. Biocraft Labs., Inc., 874 F.2d 804, 809 (Fed. Cir. 1989) (invalidating the patent on Moduretic®, a fixed-dose, combination diuretic used to treat cardiovascular and renal diseases, because the favorable interaction between the two active ingredients "was to be expected from the known natriuretic properties of the two diuretics," and therefore its therapeutic results were not "unexpectedly good"); In re Merck & Co., 800 F.2d 1091, 1097-99 (Fed. Cir. 1986) (affirming the rejection of a patent on using amitriptyline to treat depression because a medicinal chemist "would have expected amitriptyline to resemble imipramine[, a known antidepressant,] in the alleviation of depression in humans," and there was no "evidence to show that the properties of the compounds differed in such an appreciable degree that the difference was really unexpected"); In re Carabateas, 345 F.2d 1013, 1017-18 (C.C.P.A 1965) (affirming the rejection of a patent application on an analgesic that had "substantially greater analgesic effectiveness than one of the most, if not the most, active analgesic compound of the art," because the structural difference between the two drugs was known to produce greater analgesic activity in other compounds); Imperial Chemical Indus., PLC v. Danbury Pharmacal, Inc., 777 F. Supp. 330, 359-65, 369-71 (D. Del. 1991) (invalidating the patent on atenolol (Tenormin® & Tenoretic®), a beta-blocker used to treat hypertension and angina, because it found the defendant's expert witness to be more credible and persuasive than the plaintiff's witnesses on the question of "atenolol produces unexpected results, such as increased reductions in blood pressure and heart rate and a lower incidence of [central nervous system] side effects . . . as compared to other beta-blockers").

[201] Pfizer, 480 F.3d at 1371.

a policy that systematically targets the drugs created by medicinal chemists that appear most likely to be effective, and denies them patent protection.

The problem of obvious – and thus unpatentable – drugs promises to grow worse over time because the non-obviousness requirement, almost by definition, turns progress in the pharmaceutical sciences against itself; that is, it denies patent protection to new drugs based on the very advances in science that led to their discovery. In the past, the "unpredictable nature of chemical reactions" shielded most pharmaceutical patents from obviousness challenges.[202] Over the past twenty years, however, researchers have worked to reduce this uncertainty by developing more mechanistic and predictive approaches to drug discovery: ones that are less dependent on the trial-and-error process.[203] Among their successes, medicinal chemists are beginning to get better at predicting the pharmacological properties of compounds based on their structure.[204] While much progress remains to be made,[205] even now medicinal chemists often try to synthesize and test only the most promising compounds when searching for a new drug candidate, helping improve the efficiency and output of the drug discovery process.[206] Unfortunately, this more predictive approach to drug discovery comes at the expense of

[202] Eli Lilly and Co. v. Zenith Goldline Pharms., Inc., No. IP 99-38-C, 2001 WL 1397304, at *5, (S.D. Ind. Oct. 29, 2001); *see also* Bayer AG v. Carlsbad Tech., Inc., No. Civ. 01-867-B, 2001 WL 34125673, at *5 (S.D. Cal. Oct. 24, 2001); MANUAL OF PATENT EXAMINING PROCEDURE, *supra* note 94, at §§ 2144.08(e).

[203] Lawrence J. Lesko et al., *Optimizing the Science of Drug Development: Opportunities for Better Candidate Selection and Accelerated Evaluation in Humans*, 17 PHARMACEUTICAL RESEARCH 1335, 1335 (2000); *see also* PATRICK, *supra* note 131, at 1; Oliver Schwardt et al., *Drug Discovery Today*, 3 CURRENT TOPICS IN MEDICINAL CHEMISTRY 1, 1 (2003) ("The ultimate goal of drug design is [now] to reduce the empirical trial and error process in favor of a fully rational, structure-based process.").

[204] *See, e.g.*, Alex Polinsky, *High-Speed Chemistry Libraries: Assessment of Drug-Likeness*, *in* THE PRACTICE OF MEDICINAL CHEMISTRY, *supra* note 128, at 147-57; Han van de Waterbeemd & Sally Rose, *Quantitative Approaches to Structure-Activity Relationships*, *in* THE PRACTICE OF MEDICINAL CHEMISTRY, *supra* note 128, at 351-69; Camille G. Wermuth, *Specific Substituent Groups*, *in* THE PRACTICE OF MEDICINAL CHEMISTRY, *supra* note 128, at 303-25.

[205] *See generally*, Erhardt, *supra* note 192, at 17-102.

[206] *See* GARETH THOMAS, FUNDAMENTALS OF MEDICINAL CHEMISTRY 95 (2004); Camille G. Wermuth, *Application Strategies for Primary Structure-Activity Relationship Exploration*, *in* THE PRACTICE OF MEDICINAL CHEMISTRY, *supra* note 128, at 289-300.

strong patent protection,[207] since the closer an invention gets to having been produced "according to known methods" that "yield predictable results," the more likely it is to be considered "obvious."[208] As researchers develop increasingly effective ways to identify promising drug candidates without trial-and-error experimentation, the non-obviousness doctrine will likely become an ever-more serious barrier to the patentability of the drugs they discover.[209]

The Supreme Court's recent decision in *KSR International v. Teleflex Inc.* exacerbated this tension between the pharmaceutical sciences and the unexpected-results test of non-obviousness. The Court chastised the Federal Circuit for not applying the non-obviousness standard strictly enough, and made it clear that when researchers pursue "a finite number of identified, predictable solutions," one of which ultimately "leads to the anticipated success," the resulting invention is unlikely to be patentable.[210] Although drug discovery continues to involve a great deal of uncertainty,[211] this heightened

[207] Of course, if the science of medicinal chemistry were to ever reach the point where extensive clinical trials are no longer necessary, the now-inevitable clash between pharmaceutical science and the unexpected-results test of non-obviousness would disappear.
[208] KSR Int'l Co. v. Teleflex Inc., __ U.S. __ (2007).
[209] Philippe Ducor made a similar argument about technological progress in drug discovery and the non-obviousness test, although his observation focused on specific types of drug-discovery tools, and may have been mistaken about the legal effects of those technologies. *See* Ducor, supra note 176, at 435-63. Ducor, along with many others at the time, optimistically believed that high-throughput screening (an automated process of trial-and-error testing that works simultaneously on large numbers of distinct compounds) would ultimately "yield products having predetermined properties with the highest possible degree of predictability." *Id*. at 446. As a result, he concluded that the technique would "render its products . . . unpatentable due to obviousness," thereby "threaten[ing] the incentive of the pharmaceutical industry to invest in the[ir] . . . development." *Id*. at 461. In truth, because high-throughput screening is just an efficient form of blind trial-and-error experimentation, it probably shields drugs from obviousness challenges. *Cf*. Pfizer, Inc. v. Apotex, Inc., 480 F.3d 1348, 1367 (Fed. Cir. 2007). Since the individual compounds tested in the experiment do not have a reasonable likelihood of success *ex ante*, and high-throughput screening does not always identify any promising leads, *see* Wermuth, *supra* note 128, at 73-76, the drugs discovered through it will likely remain non-obvious. *Cf.* Takeda Chem. Indus. v. Alphapharm Pty., Ltd., _ F.3d _, _ (Fed. Cir. 2007) (explaining that the choice of lead compounds must have been obvious based on the prior art to support a finding of obviousness).
[210] KSR Int'l, __ U.S. at __.
[211] *See generally* Erhardt, *supra* note 192.

standard of patentability threatens to worsen an already serious problem, perhaps preventing even more drugs from being patented.[212]

As with the novelty requirement, it is impossible to know exactly how many drugs are denied patent protection as a result of the non-obviousness standard, but the problem appears to be substantial. The PTO has rejected numerous drug patents for being obvious in light of prior publications,[213] including patents on drugs for cancer,[214] HIV,[215] hypertension,[216] stroke,[217] diabetes,[218] and tuberculosis.[219] One medicinal chemistry textbook describes the non-obviousness requirement as a "significant problem in obtaining valid and effective patent protection" for drugs, and notes that that "[i]nventors' previous patents and publications often . . . [give them] difficulty patenting

---

[212] Shortly after *KSR International v. Teleflex*, several commentators predicted that the ruling would make it harder to patent certain types of new drugs. *See* Calvert D. Crary, *Impact of KSR v. Teleflex on Pharmaceutical Industry*, C.D. CRARY & CO. LITIGATION NOTES, May 2, 2007, at 1; Steven R. Ludwig & Matthew E. Kelley, *Pharmaceutical Patent Life Cycle Management after* KSR International v. Teleflex, ARTICLE (Venable LLP, Washington, D.C.), May 2007, *available at* http://www.venable.com/docs/pubs/1684.pdf.; Seema Singh, *India's Generic Drug Run: Indian Companies See an Opening for Generic Drugs in U.S.*, RED HERRING: THE BUSINESS OF TECHNOLOGY, May 15, 2007. The drug patents predicted to be most affected by *KSR* are those covering new drug formulations, controlled-release drugs, enantiomers, new salt structures of known drugs, drugs that are not first-in-class, combinations of known drugs, and minor modifications to older compounds. *See* Crary, *supra*, at 1; Ludwig & Kelley, *supra*, at 2. Of course, the true impact of KSR on pharmaceutical patents might be quite modest. Much depends on how the lower courts implement the "obvious to try" standard.

[213] *See, e.g.*, *In re Selzer*, 2007 WL 630222, at *3-6 (Bd. Pat. App. & Interf. Feb. 28, 2007); *In re Arbiser*, 2007 WL 952197, at *4-7 (Bd. Pat. App. & Interf. Feb. 6, 2007); *In re Skurkovich*, 2006 WL 1665596, at *3-8 (Bd. Pat. App. & Interf. Jan. 1, 2006); *In re Gormley*, 2004 WL 4980874, at 4 (Dec. 29, 2004); *In re Lapeurta*, 2004 WL 318776, at *2-3 (Bd. Pat. App. & Interf. Jan 1., 2004); *In re Bodmer*, 2004 WL 77132, at *2-6 (Bd. Pat. App. & Interf. 2004).

[214] *See In re Cuthbertson*, 2007 WL 1766994, at *2-5 (Bd. Pat. App. & Interf. May 24, 2007); *In re Rajopadhye*, 2007 WL 2020938, at *3-7 (Bd. Pat. App. & Interf. May 21, 2007); *In re Chen*, 2007 WL 902328, at *2-6 (Bd. Pat. App. & Interf. Mar. 16, 2007); *In re Barbera-Guillem*, 2006 WL 3502881, at *3-6 (Bd. Pat. App. & Interf. Nov. 30, 2006); *In re Shawver*, 2004 WL 4979076, at *3-5 (Bd. Pat. App. & Interf. Mar. 4, 2004); *In re Linnenbach*, 2004 WL 77144, at *2-6 (Bd. Pat. App. & Interf. Jan. 1, 2004); *In re Rosenblatt*, 2004 WL 2733627, at *3-5 (Bd. Pat. App. & Interf. Jan. 1, 2004); *In re Bianco*, 1996 WL 1799830, at *1-2 (Bd. Pat. App. & Interf. Jan. 1, 1996).

[215] *See In re Maury*, 2007 WL 2125099, at *2-7 (Bd. Pat. App. & Interf. Jul. 24, 2007); *In re Stapleton*, 2006 WL 1665384, at *3-6 (Bd. Pat. App. & Interf. 2006); *In re Williams*, 2005 WL 4773220, at *4-6 (Bd. Pat. App. & Interf. Jun. 22, 2005).

[216] *See In re Pershadsingh*, 1997 WL 1897858, at *2-5 (Bd. Pat. App. & Interf. Oct. 14, 1997) (rejecting some, but not all, of the claims to a hypertension drug as obvious).

[217] *See In re Childers*, 2003 WL 25277879, at *3-5 (Bd. Pat. App. & Interf. Dec. 22, 2003).

[218] *See In re Schmitke*, 2007 WL 2125094, at *5-6 (Bd. Pat. App. & Interf. Jul. 24, 2007).

[219] *See In re Horwitz*, 2003 WL 25283780, at *5-7 (Bd. Pat. App. & Interf. Jun. 19, 2003).

their chosen compounds because of their earlier public disclosure of compounds long since discarded."[220] The real problem is the nature of the non-obviousness requirement itself, which withholds patent protection from the drugs that appear most promising in early research, and penalizes progress in the pharmaceutical sciences. Given these strange tendencies within the doctrine, it is not surprising that drug researchers frequently encounter the non-obviousness requirement as a barrier to patenting their discoveries.

III. LOST DRUGS

More than firms in any other industry, pharmaceutical companies rely on the patent system to secure a return on their R&D investments, particularly the large investments they make in clinical trials.[221] Under the novelty and non-obviousness requirements, socially valuable drugs can be deemed unpatentable before they have been tested in those trials, and thus before they can be sold to the public. Without the patent system to incent these post-invention efforts, private industry is apt to simply ignore such drugs, likely resulting in their loss to the public. These lost drugs are nearly impossible to observe, however, since pharmaceutical companies rarely publicize the drugs that they drop from development. To determine whether the novelty and non-obviousness requirements are stifling pharmaceutical innovation, therefore, this Section examines how patents influence the R&D decision-making process inside pharmaceutical companies, finding that the patent standards routinely deter private industry from developing promising drug candidates. According to academic researchers, industry insiders, and medicinal chemistry textbooks, pharmaceutical companies systematically screen their

[220] Souleau, *supra* note 128, at 721.
[221] *See supra* text accompanying notes 21-30.

drug candidates to exclude the ones lacking strong patent protection, checking their patentability at least three different times during drug development. The existence of these screening procedures and frequency with which they influence companies' R&D investments indicates that the novelty and non-obviousness requirements are likely denying the public access to new drugs.

Pharmaceutical companies examine the patentability of their potential drug candidates at the beginning of each research project, and they regularly drop ones that appear to be in the public domain.[222] Some version of this patent screen has existed since at least the early 1960s.[223] In modern practice, company scientists often start preclinical research with a list of compounds being considered for development into a particular type of drug,[224] and their selection of compounds is often critical to the project's success.[225] According to medicinal chemistry textbooks and academic researchers, one of the first tasks performed in narrowing that list is the crossing off of any compound that the scientists think cannot be patented,[226] applying a *per se* rule that unpatentable drugs will not be developed.

---

[222] *See* Telephone Interview with Theodore Torphy, *supra* note 138 (explaining that companies evaluate the patentability of their drug candidates before advancing them into preclinical development, and that unless they are confident that a candidate can be effectively patented, they will not move forward with it).

[223] In 1962, when a change in government policy made it difficult for pharmaceutical companies to effectively patent compounds that were originally synthesized through National Institute of Health-funded research, pharmaceutical companies simply stopped screening those compounds for therapeutic activity. *See* Rebecca S. Eisenberg, *Public Research and Private Development: Patents and Technology Transfer in Government-Sponsored Research*, 82 Va. L. Rev. 1663, 1682-84 (1996). The standoff only ended when an investigation by the Comptroller General forced a change in the policy. *Id*. at 1683.

[224] *See* Malcolm MacCoss & Thomas A. Baillie, *Organic Chemistry in Drug Discovery*, 303 SCI. 1810, 1810 (2004); Mitscher & Dutta, *supra* note 40, at 108-09.

[225] *See* MacCoss & Baillie, *supra* note 224, at __.

[226] *See* George deStevens, *Lead Structure Discovery and Development*, *in* 1 COMPREHENSIVE MEDICINAL CHEMISTRY: THE RATIONAL DESIGN, MECHANISTIC STUDY & THERAPEUTIC APPLICATION OF CHEMICAL COMPOUNDS § 3.2, at 266 (Corwin Hansch ed. 1990) ("Needless to say, the lead structure series must be patentable."); Telephone Interview with Druker, *supra* note 41 (after identifying a possible lead compound, drug companies immediately check its patentability; if they discover that compound is in the public domain or has been patented by someone else, which happens frequently, standard practice is to drop the compound and look for another lead); Mitscher & Dutta, *supra* note 40, at 115; *cf*. Showell & Mills, *supra* note 137, at

In addition to this initial patent screen, pharmaceutical companies check the patentability of their drug candidates at least twice more before clinical trials, screening out any compounds with weak patent protection that escaped the prior review. Once the researchers working on a particular project have narrowed their search down to just a few drug candidates, those compounds are given to a patent attorney to evaluate their patentability and file a patent over them.[227] Later, when one of those drug candidates (hopefully) gets close to clinical trials, the firm will inspect its patent protection again, using in-house or outside counsel to perform a thorough review of the strength of its patents.[228] According to industry insiders, this last audit is considered a "gate-keeping event" before clinical trials,[229] and it is not unusual for a pharmaceutical company to sour on an otherwise promising drug candidate after their attorneys turn up a prior disclosure that threatens its patent protection.[230] These stories from industry insiders are consistent with reports from drug researchers in government and academia that private industry

551-52 ("During the lead optimization phase of projects additional factors contributing to subsequent failure may include poor portfolio decision-making and a sub-optimal IP.").

[227] *See* Janice Klunder & Sian Griffiths, A Beautiful Friendship: The Information Professional and the Patent Attorney/Agent, at 21-22 (Presentation at SLA Pharmaceutical & Health Technology Division, Spring Meeting, Boston, Mar. 19, 2007) at http://units.sla.org/division/dpht/meetings/spring2007/klunder_griffiths_2007s.ppt#270,1,Slide 1; Edlyn S. Simmons, *Prior Art Searching in the Preparation of Pharmaceutical Patent Applications*, 3 DRUG DISCOVERY TODAY 52 (1998).

[228] *See* Telephone Interview with Anonymous, Director of Intellectual Property at a mid-sized pharmaceutical company (Jan. 2007) (on file with author) (stating that companies will have thoroughly evaluated the patentability of their drug candidates roughly six to twelve months before filing an Investigational New Drug Application (INDA) with the FDA to begin clinical trials); Telephone Interview with Theodore Torphy, *supra* note 138 (explaining pharmaceutical companies use in-house or outside counsel to do a comprehensive patent search on their drug candidates during the later stages of preclinical development, before any "real money" is spent).

[229] Telephone Interview with Anonymous, Director of Intellectual Property, *supra* note 228; *see also* BARTFAI & LEES, *supra* note 135, at 113 tbl. 12.1, 135 tbl. 13.1; Telephone Interview with Theodore Torphy, *supra* note 138 (explaining that drugs found to have weak patent protection at this stage are unlikely to advance into clinical trials).

[230] *See* Telephone Interview with Anonymous, Senior Intellectual Property Counsel at a large pharmaceutical company (Jan. 2007) (on file with author) (noting that a prior disclosure will usually kill a drug project); Telephone Interview with Anonymous, Director of Intellectual Property, *supra* note 228 (explaining that the strength of patent protection influences their decision over which drug candidates to pursue, and when attorneys find a prior disclosure that weakens those patent rights, companies are much less likely to develop the drug).

refuses to take over the development of their drugs without a patent,[231] and reports from venture capitalists that strong patent portfolios are a prerequisite for investing in biotechnology companies.[232] A basic adage in the pharmaceutical industry is that drugs without strong patent protection are not worth developing,[233] and the purpose of these screening mechanisms is to ensure that companies do not move forward on a drug candidate unless their patents over it are secure.[234]

The screening procedures used by pharmaceutical companies are generally focused on a drug's patentability in the United States, and thus exclude drugs from development that lack U.S. patent coverage even if they can be protected in other countries. In the global drug market, roughly half of industry profits come from sales in the United States.[235] (The other major markets, France, Germany, Italy, Spain, Japan, and the United Kingdom, generate a much smaller share of sales.[236]) As a result, private industry will screen drugs out of development based solely on their lack of patentability in the United States, paying little attention to the opportunities for protection elsewhere.[237]

---

[231] *See* supra note 41.

[232] *See, e.g.*, Suzanne Berry, *Biotech Meets the Investors*, 20 TRENDS IN BIOTECHNOLOGY 370, 371 (2002); *Hans Kupper Discusses Science and Venture Capital, Interview by Joanna Pinto*, 9 DRUG DISCOVERY TECH. 909, 911 (2004).

[233] *See* BARTFAI & LEES, *supra* note 135, at 135; Fredric J. Cohen, *Macro Trends in Pharmaceutical Innovation*, 4 NATURE REV. DRUG DISCOVERY 78, 80 (2005); Gwynne & Heebner, *supra* note 40, at 2086; Mitscher & Dutta, *supra* note 40, at 104, 115; SCHACTER, *supra* note 40, at 52.

[234] Pharmaceutical companies also rely on these reviews to find patents held by other firms that they might infringe if they were to develop the drug candidate. *See* Telephone Interview with Theodore Torphy, *supra* note 138; Warren D. Woessner, Preparing Patent Legal Opinions 2006, *in* PREPARING PATENT LEGAL OPINIONS 2006, at 85-105 (PLI Pats., Copyrights, Trademarks, and Literary Prop. Course, Handbook Series No. 8996, 2006), WL 876 PLI/Pat 77.

[235] Press Release, IMS Health Inc., Global Pharmaceutical Sales by Region, 2006 (Mar. 20, 2007) (on file with author).

[236] Japan generates less than 10% of total global pharmaceutical sales, and the five major European markets, France, Germany, Italy, Spain and the U.K., together account for less than 20%. *See* Press Release, IMS Health Inc., IMS Health Reports Global Pharmaceutical Market Grew 7.0 Percent in 2006, to $643 Billion (Mar. 20, 2007) (on file with author).

[237] *See* BARTFAI & LEES, *supra* note 135, at 138.

For most of these discarded drugs, the reason why their patent protection is inadequate relates either directly or indirectly to the novelty and non-obviousness requirements.[238] As discussed in Part II, prior publications that describe a drug or cause it to appear obvious can prevent anyone from later patenting it.[239] Those prior disclosures sometimes leave room for a narrow patent on the drug,[240] but many times those patents are ineffective[241] because their limited scope would allow competitors to launch generics without infringing the patent.[242] Although pharmaceutical companies can occasionally block those generics by arguing that they are functionally equivalent to what was claimed in their patent,[243] courts are reluctant to apply this doctrine of

[238] The novelty and non-obviousness requirements define the scope of the public domain, and are therefore the only doctrines that can prevent a valuable drug from being patented. Courts and the PTO sometimes reject or invalidate drug patents based on other doctrines, including the utility and enablement requirements. *See* Cooper, *supra* note 98; THOMAS, *supra* note 94, at 60-83, 204-08. Without the novelty and non-obviousness requirements, however, these failings could be corrected in a subsequent patent filing (unless the drug has no utility or cannot be manufactured or used, in which case it is of no consequence).

[239] *See supra* text accompanying notes 119-147, 213-220.

[240] *See* Simmons, *supra* note 227, at 54.

[241] *See, e.g.*, Astrazeneca AB v. Mutual Pharm. Co., 384 F.3d 1333, 1341-42 (2004); Abbott Labs. v. Novopharm Ltd., 323 F.3d 1324, 1331 (2003); Novartis Corp. v. Ben Venue Labs., Inc., 271 F.3d 1043 (2001); Biovail Corp. Int'l v. Andrx Pharms., Inc., 239 F.3d 1297, 1301-03 (2001).

[242] Certain types of drug patents are particularly vulnerable to these design-around efforts, while others are not. If a drug only has one active ingredient and that ingredient is patented, then the patent will be difficult for generics to design around even if it is narrow, since any change the generic firms make to the active ingredient would likely trigger the FDA's clinical trial requirements. *See* 21 C.F.R. § 314.93. Similarly, if a pharmaceutical company has a patent on the only FDA-approved use for a drug, then generic manufacturers cannot receive FDA approval to sell that drug for its approved use without infringing the patent. *See* MARTIN A. VOET, THE GENERIC CHALLENGE: UNDERSTANDING PATENTS, FDA & PHARMACEUTICAL LIFE-CYCLE MANAGEMENT 36-38 (2005). If the novelty or non-obviousness requirement make it impossible to patent a drug's active ingredient or the medical use(s) for which it will be approved, *see, e.g.*, *supra* notes and text accompanying notes 80-89, 100-103, 140-147, 191-198, and 210-217, then firms can sometimes receive a narrower patent, such as one on a particular crystalline or salt form of the drug, a route of administering it (including the addition of other ingredients to the drug that affect its absorption, distribution or metabolism in the body), and particular dosage forms or strengths of the drug. *See* VOET, *supra*, at 35-39. Unlike patents on a drug's active ingredient or its FDA-approved uses, however, these narrower patents are often vulnerable to being designed around by generic manufacturers, since the FDA will allow generics onto the market that are "not identical to [the] listed drug in route of administration, dosage form, and strength" so long as it believes the differences will not effect the safety and effectiveness of the drug. 21 C.F.R. §§ 314.93(b), (e)(1)(i).

[243] *See Abbott Labs. v. Dey, L.P.*, 287 F.3d 1097, 1105-07 (2002).

equivalents,[244] and it can only be used when the novelty and non-obviousness requirements would not have prevented the patent claims from encompassing the generic.[245] Moreover, pharmaceutical companies are often estopped from invoking that doctrine by their own prior statements to the PTO, where they had to interpret their patent claims narrowly to overcome a PTO rejection for obviousness or lack of novelty.[246] Similar problems can arise if the pharmaceutical company failed to inform the PTO of a prior reference that was material to their drug's novelty or non-obviousness.[247] Deliberately withholding such a reference from the PTO is considered inequitable conduct and can render the patent unenforceable, even when the patent is valid.[248] Concerns over the patent protection on a drug related to any of these doctrines are likely to result in it being considered unpatentable, and thus liable to be screened out of development.

Although unpatentable drugs occasionally slip through the pharmaceutical companies' screening procedures and are developed despite such inadequacies in their patent protection, given the careful efforts by pharmaceutical companies to prevent this from happening, it is likely that the vast majority of those drugs never reach the public. As seen in the cases discussed in Part II, pharmaceutical companies sometimes develop and market new drugs with patents that the courts later invalidate for lack of novelty or

---

[244] *See* Charles W. Adams, *The Doctrine of Equivalents: Becoming a Derelict on the Waters of Patent Law*, 84 NEB. L. REV. 1113, 1113-14 (2006); John R. Allison & Mark A. Lemley, *The (Unnoticed) Demise of the Doctrine of Equivalents*, 59 STAN. L. REV. 955 (2007); John R. Thomas, *Claim Re-Construction: The Doctrine of Equivalents in the Post-Markman Era*, 87 J. PAT. & TRADEMARK OFF. SOC'Y 781, 783-89 (2005).

[245] *See* Ortho-McNeil Pharm., Inc. v. Caraco Pharm. Labs., Ltd., 476 F.3d 1321, 1328-29 (2007); Merck & Co. v. Mylan Pharm. Inc., 19 F. Supp. 2d 334, 340-47 (1998).

[246] *See, e.g.*, Schwarz Pharma, Inc. v. Paddock Labs., Inc., 504 F.3d 1371, 1375-78 (2007); Pharmacia & Upjohn Co. v. Mylan Pharm. Inc., 170 F.3d 1373, 1376-79 (1999).

[247] *See* Purdue Pharma L.P. v. Endo Pharms. Holding Inc., 438 F.3d 1123 (2006); Aventis Pharma S.A. v. Amphastar Pharms., Inc., 390 F.3d 936 (2005).

[248] *See* Hoffman-La Roche Inc. v. Lemmon Co., 906 F.2d 684, 687-88 (1990).

obviousness.[249] In most of these cases, however, the drugs at issue were developed before generic manufacturers started to aggressively challenge pharmaceutical-company patents in the mid-1990s,[250] and thus before it became crucial for drugs to be protected by a *valid* patent. Pharmaceutical companies are now more vigilant in policing their own patents, and with the advent of the internet and browsing technology, it has become much easier for the firms to locate prior disclosures.[251] In this environment, private industry is unlikely to make many mistakes, and drugs with weak patent protection will rarely enter clinical trials.

When a drug is screened out of development under these circumstances, the resulting loss to the public is unlikely to be mitigated by the gain of some other drug developed in its place. Good drugs are hard to find,[252] and firms cannot easily identify patentable drugs of comparable quality to replace the unpatentable ones they discard.[253]

---

[249] *See supra* notes 100-104, 109-111, 200.

[250] *See* GENERIC DRUG ENTRY PRIOR TO PATENT EXPIRATION: AN FTC STUDY 10, 57 (Federal Trade Commission, 2002). Up until the late 1990s, FDA regulations made it difficult for generic drug companies to receive the 180-day period of generic exclusivity intended to reward them for successfully challenging a drug patent. *See* ERNST R. BERNDT ET AL., DO AUTHORIZED GENERIC DRUGS DETER PARAGRAPH IV CERTIFICATIONS? RECENT EVIDENCE 5 (Apr. 17, 2007) *at* http://www.analysisgroup.com/analysisgroup/uploadedFiles/Publishing/Articles/PhRMA_Authorized_Generic_Entry.pdf. In fact, between 1984 and 1997, there were only three occasions when the FDA granted a 180-day exclusivity period to a generic-drug company. *See* GENERIC DRUG ENTRY PRIOR TO PATENT EXPIRATION, *supra*, at 57. Not surprisingly, generic companies initiated relatively few challenges on pharmaceutical company patents during those years. *See id*., at 10; BERNDT ET AL., *supra*, at 19 exh.3. Starting in 1997, however, when a federal district court struck down the FDA's interpretation of the statute regarding the grant of 180-day exclusivity periods, *see* Mova v. Shalala, 955 F. Supp. 128 (D.D.C. 1997), *aff'd*, 140 F.3d 1060 (D.C. Cir. 1998), the number of generic challenges to pharmaceutical patents increased dramatically. *See* GENERIC DRUG ENTRY PRIOR TO PATENT EXPIRATION, *supra*, at 10; BERNDT ET AL., *supra*, at 19 exh.3. Those challenges are now so commonplace that the patents on successful new drugs are almost guaranteed to end up in litigation. *See* Alicia Ault, *Generic Drugs: A Big Business Getting Bigger*, THE SCIENTIST, at 36 (June 20, 2005); Bruce N. Kuhlik, *The Assault on Pharmaceutical Intellectual Property*, 71 U. CHI. L. REV. 93, 102 (2004).

[251] *See* Telephone Interview with Declan Doogan, M.D., President of Research and Development at Amarin, London, U.K. (Jan. 25, 2007) (on file with author) (explaining that browsing technology makes it much easier for pharmaceutical companies to find patent-busting literature on their own products).

[252] *See* NATIONAL INSTITUTE OF HEALTH, RESPONSE TO THE CONFERENCE REPORT REQUEST FOR A PLAN TO ENSURE TAXPAYERS' INTERESTS ARE PROTECTED _ (2001).

[253] During early preclinical research, when company scientists are trying to select a drug candidate for further testing among a list of numerous compounds, each of which performed similarly in an initial

Moreover, unless two drugs are so closely related as to be therapeutic substitutes, it is unclear why firms would shift resources over from an unpatentable drug to a patentable one. The R&D side of the pharmaceutical industry is highly competitive,[254] and firms should be expected to pursue all drug candidates with anticipated net positive returns, not just the drugs with the highest anticipated net returns. Unless firms in the pharmaceutical industry are for some reason unable to borrow money or are experiencing long-term labor shortages,[255] their decisions to drop a particular drug from development due to weak patent protection should have little effect on their decisions to develop other types of drugs. When pharmaceutical companies screen unpantentable drugs out of their pipeline, therefore, the public should not expect to receive other drugs in their place. The loss of an unpatentable drug is simply that, a loss.

The social costs of losing such drugs likely far outweigh any benefits to the public from faster access to inexpensive generics of the unpatentable drugs that actually reach the market. As noted above, pharmaceutical companies rigorously screen the drugs in their pipeline to exclude ones with weak patent protection, which suggests that the vast

---

laboratory experiment, the scientists are likely to move forward with a compound from the list even if the most promising ones were ruled out as unpatentable. *See supra* text accompanying notes 222-226. On many occasions, however, there is no second-best alternative. *See* David J. Payne et al., *Drugs for Bad Bugs: Confronting the Challenges of Antibacterial Discovery*, 6 NATURE REVIEWS: DRUG DISCOVERY 29, 31-33 (2007). Moreover, even if a second or third-choice compound is available, by forcing the firm to work on a more flawed compound, the patent system is significantly reducing the probability of ultimate success in producing a safe and effective drug. "Indeed, finding a suitable starting molecule is often the most challenging feature of the search" for new drugs. Mitscher & Dutta, *supra* note 40, at 104.

[254] *See* Scherer, *supra* note 18, at 29-33.

[255] It is unlikely that drug development is being stymied by a shortage of capital in the pharmaceutical industry. Although capital restraints might cause a pharmaceutical company to treat drug candidates as competing investment opportunities within a single budget year, *see* BARTFAI & LEES, *supra* note 135, at 58, those firms have access to the capital markets, and generally have good credit ratings. *See* Standard & Poor's, *A Better Prognosis for Big Pharma*, BUSINESS WEEK ONLINE, May 4, 2006, at 12. Consequently, pharmaceutical companies should be expected to adjust their annual budgets, if need be by borrowing money, to ensure that they can develop all of the profitable drugs identified by their researchers. If pharmaceutical companies are leaving profitable drugs on the table, it is likely because they lack the human capital necessary for pursuing all of the profitable drugs in their pipeline. In the long run, however, the demand for workers *should* lead more people to enter the industry.

majority of those drugs are never made available to the public.[256] Of course, some unpatentable drugs are developed despite their lack of protection, sometimes because the manufacturer mistakenly believed that the drug was adequately covered by a patent,[257] and sometimes because of unusual circumstances under which it is profitable to develop the drug without patent protection.[258] If these drugs had been patented, it would have taken years longer for generics to enter the market, and consumers would have suffered. So long as private industry screens the bulk of unpatentable drugs out of development, however, the harm caused by their loss likely dwarfs any benefits from faster access to generics.[259]

The magnitude of this injury is generally hidden from the public as a result of the early stage at which most unpatentable drugs are screened out of development.

---

[256] *See supra* text accompanying notes 222-234, 249-251.

[257] *See supra* notes and text accompanying notes 80-89 (discussing the development of Ultracet®). Mistakes such as these are likely rare, however, since pharmaceutical companies use redundant checks – at least three independent reviews – to screen out unpatentable drugs. *See supra* text accompanying notes 222-234. When companies mistake a patentable drug for an unpatentable one, however, there are no built-in redundancies to prevent those drugs from being discarded. As a result, there should be far fewer instances of firms unwittingly developing an unpatentable drug compared with mistakes made in excluding patentable drugs. On balance, therefore, these mistakes likely harm the public.

[258] Pharmaceutical companies are *sometimes* willing to develop so-called "orphan drugs" without patent protection, since they cost less to develop and market and are guaranteed seven years of marketing exclusivity. New drugs receive "orphan" status if they are approved for the treatment of "rare diseases or conditions," which Congress defined as ones "affect[ing] less than 200,000 persons in the United States," or ones "for which there is no reasonable expectation that the cost of developing . . . a drug for such a disease or condition will be recovered from sales." 21 U.S.C. § 360bb(a)(2). Once a drug receives orphan status, the FDA will "not approve another application . . . for such drug for such disease or condition . . . until the expiration of seven years from the date of approval of the approved application." *Id*. at § 360cc(a). Compared with other drugs, orphan drugs are typically less expensive to develop because they require fewer clinical trials to secure FDA approval, complete their clinical trials over a year earlier on average, and are approved faster by the FDA. *See* Christopher-Paul Milne, *Orphan Products—Pain Relief for Clinical Development Headaches*, 20 NATURE BIOTECHNOLOGY 780, 782 (2002). Moreover, because orphan drugs are generally prescribed by a small group of specialty physicians and have little competition from existing therapies, they cost much less to commercialize than ordinary drugs. *See id*. at 783. As a result, industry executives report that private industry is sometimes willing to develop an orphan drug with only the seven-year period of market exclusivity. *See* Telephone Interview with Anonymous, Senior Intellectual Property Counsel, *supra* note 230 (noting that for drugs that treat rare diseases, the seven years of marketing exclusivity provided under the Orphan Drug Act is sometimes enough for the company to move forward); Telephone Interview with Declan Doogan, *supra* note 251 (same).

[259] *See supra* text accompanying note 36.

Pharmaceutical companies do not announce the drug candidates that they choose not to develop, including the ones dropped on account of a prior disclosure which undermined their patent protection. While industry insiders acknowledge that many such drugs exist,[260] the decisions to discard them are made behind closed doors. On occasion the public might catch a glimpse of one of these drugs, such as when the PTO rejects a drug-patent application for lack of novelty or obviousness. These PTO decisions, of which there have been many,[261] can end private industry's efforts to develop the claimed drug.[262] Even under these circumstances, however, the injury to the public is usually obscured by the absence of clinical-trial data on the drug's safety and efficacy,[263] preventing the public from knowing which of the drugs ultimately would have been approved by the FDA and how valuable those drugs would have been. The public-health

[260] *See* Telephone Interview with Anonymous, Director of Intellectual Property, *supra* note 228; Telephone Interview with Anonymous, Senior Intellectual Property Counsel, *supra* note 230; *cf.* Telephone Interview with Druker, *supra* note 41 (commenting as an academic researcher who has worked with private industry).

[261] *See, e.g.*, In re Ames, 2007 WL 1033514 (Bd. Pat. App. & Interf. Mar. 28, 2007); In re Selzer, 2007 WL 630222, at *3-6 (Bd. Pat. App. & Interf. Feb. 28, 2007); In re Arbiser, 2007 WL 952197, at *4-7 (Bd. Pat. App. & Interf. Feb. 6, 2007); In re Skurkovich, 2006 WL 1665596, at *3-8 (Bd. Pat. App. & Interf. Jan. 1, 2006); In re Gormley, 2004 WL 4980874, at 4 (Dec. 29, 2004); In re Bhagwat, 2004 WL 366282, at *4 (Bd. Pat. App. & Interf. Jan. 6, 2004); In re Lapeurta, 2004 WL 318776, at *2-3 (Bd. Pat. App. & Interf. Jan 1., 2004); In re Bodmer, 2004 WL 77132, at *2-6 (Bd. Pat. App. & Interf. 2004); In re Feldmann, 2003 WL 25281968, at *2-4 (Bd. Pat. App. & Interf. Mar. 21, 2003); In re Saito, 1999 WL 33230062, at *5-6 (Bd. Pat. App. & Interf. Jun. 9, 1999); In re Flowers, 1994 WL 1709509 (Bd. Pat. App. & Interf. Sept. 22, 1994).

[262] When the PTO rejects a patent application on a drug for lack of novelty, it does not necessarily mean that the applicant will drop its research into the claimed drug, since the applicant may have other ways of securing patent protection over the drug. For example, in *In re Hofmann*, the PTO rejected the claims on a compound for treating HIV, but allowed the claims on a method of using that compound for the treatment of HIV. 1999 WL 33548892, at *4-5 (Bd. Pat. App. & Interf. Sept. 14, 1999). Although these method-of-use patents are considered weaker than a patent on the compound itself, *see* Anton Hopen, *Intellectual Property in Drug Development: A Report from a Breakout Session*, 25 RETINA S95 (2005), and pharmaceutical companies are more likely to develop a drug when they have a patent on its active ingredient, *see* SCHACTER, *supra* note 40, at 50, method-of-use patents can provide sufficient protection to allow companies to develop the drug. *See* VOET, *supra* note 242, at 35-39. In many of the PTO decisions cited above and throughout the article, however, the rejections encompassed the method of using the claimed drug, which often leaves little room for pharmaceutical companies to draft an effective patent.

[263] *See, e.g.*, AVORN, *supra* note 113, at 39-68; Barry L. Beyerstein, *Alternative Medicine and Common Errors of Reasoning*, 76 ACAD. MED. 230 (2001).

consequences of the novelty and non-obviousness requirements thus remain largely unobservable.

There can be exceptions, of course, such as when the government funds its own clinical trials on an unpatentable drug, providing evidence of health benefits the public would have been receiving if private industry had developed the drug earlier. One notable example involves the drug finasteride and its use in the prevention of prostate cancer. The PTO held that this use for the drug was not novel because finasteride had already been developed as a treatment for benign enlarged prostates,[264] and anyone who used it for that purpose would inherently (*i.e.*, unknowingly) benefit from its chemopreventative effects.[265] With little incentive for pharmaceutical companies to invest in this newly-discovered yet non-novel therapy,[266] the National Cancer Institute stepped in and funded its own clinical trial,[267] demonstrating that finasteride reduces the

[264] The FDA approved finasteride as a treatment for benign prostatic hyperplasia, although it is not widely prescribed for that purpose. *See* Christopher S. Saigal et al., *Economic Evaluation of Treatment Strategies for Benign Prostatic Hyperplasia – Is Medical Therapy More Costly in the Long Run?*, 177 J. UROLOGY 1463, 1464 (2007) (finding that less than 10% of patients treated for benign prostatic hyperplasia are given finasteride).

[265] In re Gormley, 2001 WL 1049136, at *3-4 (Bd. Pat. App. & Interf. 2001) (explaining that the mere discovery of "a new benefit of an old process cannot make the process again patentable"). The PTO has rejected other drug patents on the same grounds of inherent anticipation, including an HIV drug and a drug for raising HDL ("good") cholesterol levels. *See* In re Williams, 2005 WL 4773220, at *4 (Bd. Pat. App. & Interf. Jun. 22, 2005); In re Levin, 2004 WL 1697793, *2-4 (Bd. Pat. App. & Interf. 2004).

[266] Without patent protection, private industry was unlikely to ever fund clinical trials on finasteride's chemopreventative benefits. Even with a patent, however, industry would probably be reluctant to fund those trials without significant financial support from the public sector. *Cf.* Ronald B. Herberman et al., *Cancer Chemoprevention and Cancer Preventive Vaccines—A Call to Action: Leaders of Diverse Stakeholder Groups Present Strategies for Overcoming Multiple Barriers to Meet an Urgent Need*, 66 CANCER RES. 11540 (2006) (discussing the various barriers to private investment in chemoprevention). Clinical trials on chemopreventative drugs are not only expensive; they also take about five years longer on average than most other clinical trials, which shortens their effective patent life, and thus deters pharmaceutical companies from developing them. *See id*. at 11546-48. With a patent, however, private industry might have invested in further clinical trials to resolve unanswered questions about the drug and market it to physicians.

[267] *See* Press Release, National Cancer Institute, First Prostate Cancer Prevention Drug Found, But Not All Men Benefit: NCI Announces Results of Prostate Cancer Prevention Trial (Jun. 24, 2003), *at* http://www.cancer.gov/newscenter/pressreleases/PCPTresults.

incidence of prostate cancer in men age 55 years and older by almost 25 percent.[268] Although there were concerns at first that finasteride might increase the risk for high-grade prostate cancer,[269] recent studies suggest the opposite,[270] and experts have grown increasingly confident that wider use of finasteride would significantly reduce the morbidity and mortality caused by prostate cancer.[271] Publicly-funded research of this sort is often slow to influence physician practices,[272] however, and the concerns over high-grade cancer still deter most physicians from prescribing finasteride as a prophylactic.[273] While a pharmaceutical company would likely have greater success in promoting finasteride,[274] none of them have an incentive to fund studies that would resolve lingering questions about the drug's safety, seek FDA approval for its use in

---

[268] *See* Ian M. Thompson et al., *The Influence of Finasteride on the Development of Prostate Cancer*, 349 NEW ENG. J. MED. 215 (2003).

[269] *See* Philip Kantoff, *Prevention, Complementary Therapies, and New Scientific Developments in the Field of Prostate Cancer*, 8 REVIEWS IN UROLOGY S9, Supp. 2, at S10 (2006); Peter T. Scardino, *The Prevention of Prostate Cancer – The Dilemma Continues*, 349 NEW ENG. J. MED. 297 (2003).

[270] *See* Vahagn R. Ashughyan et al., *Chemopreventive Trials in Urologic Cancer*, 8 REVIEWS IN UROLOGY 8, 12 (2006); Charles Bankhead, *New Finasteride Trial Results Aim to Curb Controversy*, 98 J. NAT'L CANCER INST. 1104, 1105 (2006); Anthony V. D'Amico & Claus G. Roehrborn, *Effect of 1mg/day Finasteride on Concentrations of Serum Prostate-Specific Antigen in Men with Androgenic Alopecia: A Randomized Controlled Trial*, 8 LANCET ONCOLOGY 21, 24 (2007); Ian M. Thompson et al., *Effect of Finasteride on the Sensitivity of PSA for Detecting Prostate Cancer*, 98 J. NAT'L CANCER INST. 1128, 1133 (2006); JF Thorpe et al., *A Review of Phase III Clinical Trials of Prostate Cancer Chemoprevention*, 89 ANNALS ROYAL C. SURGEONS ENG. 207, 208, 209-10 (2007).

[271] *See, e.g.*, Edith Canby-Hagino et al., *Looking Back at PCPT: Looking Forward to New Paradigms in Prostate Cancer Screening and Prevention*, 51 EUR. UROLOGY 27, 32 (2007); Yair Lotan et al., *Implications of the Prostate Cancer Prevention Trial: A Decision Analysis Model of Survival Outcomes*, 23 J. CLINICAL ONCOLOGY 1911, 1919 (2005); Mark A. Rubin & Philip W. Kantoff, *Effect of Finasteride on Risk of Prostate Cancer: How Little we Really Know*, 91 J. CELLULAR BIOCHEMISTRY 478, 482 (2004).

[272] *See* Robert L. Frye et al., *Gap Between Clinical Trials and Clinical Practice: Lessons from the Bypass Angioplasty Revascularization Investigation (BARI)*, 107 CIRCULATION 1837, 1837, 1839 (2003); Elana Hayasaka, *President's Cancer Panel Suggests Ways to Accelerate Cancer Treatment Advancements*, 97 J. NAT'L CANCER INST. 956 (2005); *cf.* AVORN, *supra* note 113, at 269-272 (discussing some of the difficulties physicians face in keeping up with the constant flood of new research on drugs).

[273] *See* Bankhead, *supra* note 270, at 1104; Sarah L. Zielinski, *Despite Positive Studies, Popularity of Chemoprevention Drugs Increasing Slowly*, 96 J. NAT'L CANCER INST. 1410, 1410 (2004).

[274] *Cf.* Robert W. Dubois, *Pharmaceutical Promotion: Don't Throw the Baby Out with the Bathwater*, W3 HEALTH AFF. 96, 99 (2003); Michael Privitera, *Large Clinical Trials in Epilepsy: Funding by the NIH Verses Pharmaceutical Industry*, 68 REVIEWS/EPILEPSY RES. 52, 56 (2006). Pharmaceutical companies are in the business of influencing physician practices, and for better or worse, they are very good at it. *See, e.g.*, AVORN, *supra* note 113, at 292-312.

preventing prostate cancer, or market the therapy to physicians. Without these commercialization efforts, it may be years before the medical community reaches a consensus on the appropriate role for this unpatentable therapy.[275]

Whenever the patent rules prevent the introduction of a new drug or therapy, or even just delay it, as may be happening with finasteride, the injury to the public can be severe. Over two hundred thousand men will be diagnosed with prostate cancer in the United States this year, and over twenty-seven thousand will die from the disease.[276] If finasteride works as many experts anticipate, then the current delay in its use could be causing thousands of unnecessary deaths.[277] This is not the only example of a potentially valuable but unpatentable therapy the public is not using. Untold numbers of other drugs have been screened out of development by pharmaceutical companies for reasons related to their patentability, perhaps including drugs for HIV, cancer, heart disease, stroke, diabetes, malaria, tuberculosis and diarrhea[278] – conditions that afflict and kill millions of people each year.[279] Losing an effective treatment for any one of those conditions would be a tragedy, even if it offers only minor improvements in health outcomes.

The public relies on the patent system to promote pharmaceutical innovation; encouraging not just the invention of new drugs, but also their development and commercialization. When the system fails, and private industry is given little incentive to

---

[275] *See* Telephone Interview with Ian M. Thompson, M.D., Professor at the University of Texas Health Science Center at San Antonio, Chairman of the Department of Urology (Nov. 27, 2006) (on file with author).
[276] *See* AMERICAN CANCER SOCIETY, CANCER FACTS & FIGURES 2007, at 4 (2007).
[277] *See* Joseph M. Unger et al., *Estimated Impact of the Prostate Cancer Prevention Trial on Population Mortality*, 103 CANCER 1375, 1380 (2005).
[278] *See supra* notes 141-147, 214-219.
[279] *See* JOINT UNITED NATIONS PROGRAM ON HIV/AIDS & WORLD HEALTH ORGANIZATION, AIDS EPIDEMIC UPDATE: DECEMBER 2006, at 1 (2006); Alan D. Lopez et al., *Global and Regional Burden of Disease and Risk Factors, 2001: Systematic Analysis of Population Health Data*, 367 LANCET 1747, 1751 (2006); WORLD HEALTH ORGANIZATION, PREVENTING CHRONIC DISEASES: A VITAL INVESTMENT 3, 6 (2005).

invest in developing and marketing a potentially valuable new drug, the public can suffer a tremendous loss. The widespread practice among pharmaceutical companies of screening their drug candidates to remove ones with insufficient patent protection indicates that these loses are likely real. Current patent policy, which withholds patent protection from drugs because they lack novelty or are obvious, therefore poses a substantial threat to the public's wellbeing.

IV. SOLUTIONS

Patent reform is now a popular subject among scholars and policymakers, but the calls for reform rarely seek additional protections for pharmaceuticals.[280] Indeed, the pharmaceutical industry is thought to be one of the few places where the patent system is effective at promoting innovation.[281] Since the patent system seems to be failing for many other industries,[282] several scholars have suggested adopting technology-specific patent rules to deal with the distinct attributes of different technologies.[283] Others favor a system of unitary patent laws and often advocate stricter enforcement of the existing patent standards.[284] With rare exception,[285] however, neither side of this debate has

[280] *See* Robert A. Armitage, *The Conundrum Confronting Congress: The Patent System Must Be Left Untouched While Being Radically Reformed*, 5 J. MARSHALL REV. INTELL. PROP. L. 268, 268-73 (2006); Clarisa Long, *Our Uniform Patent System*, 55 FED. LAW. 44, 45-47 (2008).
[281] *See* Armitage, *supra* note 280; BESSEN & MEURER, *supra* note 1, at 14-16; JAFFE & LERNER, *supra* note 1, at 39-41; SCHERER, *supra* note 39. The most common call for drug-patent reform is to crackdown on patent evergreening, where firms try to extend the patent lives on their drugs. *See, e.g.*, Burk & Lemley, *supra* note 21, at 1687; SCHERER, *supra* note 39, at 50.
[282] *See* BESSEN & MEURER, *supra* note 1, at 14-16; SCHERER, *supra* note 39.
[283] *See, e.g.*, Peter S. Menell, *A Method for Reforming the Patent System*, Berkeley Center for Law and Technology: Law and Technology Scholarship, Paper 34 (May 3, 2007) *at* http://repositories.cdlib.org/bclt/lts/34; William Fisher, *The Disaggregation of Intellectual Property: How the Laws of Intellectual Property have Grown – and Grown Apart*, HARVARD LAW BULLETIN (Summer 2004); *cf*. Burk & Lemley, *supra* note 21, at 1634-38.
[284] *See* JAFFE & LERNER, *supra* note 1, at 203-05; Long, *supra* note 280.
[285] *See infra* note 292.

focused on ways of improving the patent system for drugs,[286] believing that its role in identifying and rewarding valuable drugs is largely a success story and (except for some concerns over "evergreening" patents)[287] should be left untouched.[288] Scholars have overlooked how the patent standards suppress pharmaceutical innovation by limiting patents to innovative new ideas for drugs, such that the system offers no incentive for the development of socially valuable drugs that were disclosed or made to look promising in earlier publications.

Congress has several tools at its disposal for encouraging the development of these drugs, including patent-law reforms, direct government funding of clinical trials, and, most promisingly, market-exclusivity awards enforced through the FDA. Part A of this section outlines changes to the novelty and non-obviousness requirements that would prevent drugs from falling into the public domain prematurely, noting several drawbacks to this approach. Part B discusses Congress' possible role in financing the development of unpatentable drugs, and how presently the government is generally incapable of successfully prosecuting this task. Part C argues that the best way to motivate the development of unpatentable drugs is through FDA regulations. Although pharmaceutical companies now rely on the patent system to recoup their R&D investments, typically requiring ten or more years of market exclusivity on the products they develop,[289] the FDA could provide this same period of exclusivity by simply postponing its regulatory approval of generics. Since the FDA's clinical-trial

[286] *See supra* note 280.
[287] *See supra* note 115.
[288] *See* Armitage, *supra* note 280. *Cf.* BESSEN & MEURER, *supra* note 1; SCHERER, *supra* note 39.
[289] *See* Telephone Interview with Anonymous Director of Intellectual Property, *supra* note 228 (explaining that firms typically invest in a new drug only if they expect at least ten years of marketing exclusivity); *cf.* Grabowski, *supra* note 38, at 20.

requirements are the reason why firms rarely develop drugs without protection from generic competitors, FDA-administered exclusivity periods link the reward of exclusivity with the need for that protection, offering a convenient fix for the patent system's inadequacies in promoting drug development.

A. Patent Reform

Perhaps the most obvious solution to the problem of unpatentable drugs is to make those drugs patentable again. Congress could carve out an exemption in the novelty and non-obviousness standards for drugs that must be proven safe and effective in clinical trials before they can be sold to the public.[290] This legislative response would likely have costs, however. Such a dramatic change in the novelty and non-obviousness requirements might open the door to abusive patenting strategies, and could even be considered unconstitutional under current Supreme Court precedent. More modest reforms in the patent standards might avoid these problems, but would only help to incent the development of a much smaller group of drugs. Patent reforms are therefore a second-best solution.

To address the problem caused by the novelty and non-obviousness standards, Congress could amend those rules to ensure that drugs can be patented if they must still complete the FDA's clinical trial requirements. With respect to the novelty requirement, it could carve out an exception that allows researchers to patent drugs that have not yet been developed and are not otherwise covered by a valid patent or pending patent

[290] Congress adopted a version of this approach for certain biologic drugs in 1996, inserting a special provision in the non-obviousness statute to safeguard the patentability of particular biotechnological processes. *See* 35 U.S.C. § 103(b).

application.[291] The non-obviousness requirement could be similarly adjusted to provide that a drug is not obvious unless there is no longer any need for it to be tested in rigorous clinical trials to satisfy the FDA's safety and efficacy standards. Indeed, Congress could explicitly tie the non-obviousness standards for pharmaceutical patents to the FDA's regulatory requirements, such that a drug is non-obvious if it must complete the full panoply of FDA-required clinical trials before the public can benefit from its use.[292] In circumstances where the FDA will approve a new drug based almost entirely on clinical-trial data submitted for another drug, as it does with generics and certain formulation changes in existing drugs, then the traditional non-obviousness test (or perhaps a much stricter one) would be appropriate.

One problem with these proposals for amending the novelty and non-obviousness requirements is that they might be difficult to implement without inadvertently allowing firms to engage in abusive patenting strategies. Both requirements play an important role

---

[291] It is possible that this rule might violate the TRIPS Agreement, which states that "patents shall be available and patent rights enjoyable without discrimination as to . . . the field of technology." Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), Apr. 15, 1994, art. 27(1), 33 I.L.M. 81, 93-94; *see* Burk & Lemley, *supra* note 21, at 1678. Nonetheless, the United States patent laws already contain certain industry-specific provisions designed to benefit the pharmaceutical industry, such as an exemption in the non-obviousness requirement for certain types of biotechnology patents, *see* 35 U.S.C. § 103(b), and patent-term extensions for pharmaceuticals, *see* 35 U.S.C. § 156. The reason why these provisions have not yet been challenged is likely because the TRIPS provision can only be enforced through the World Trade Organization's (WTO) dispute resolution procedures, which require a challenge from another member country. *See* TRIPS Agreement, art. 64(1). The only remedy the WTO can provide is to authorize the challenger to impose trade sanctions against the violating member. *See id*. With respect to the law proposed above, which would exempt certain pharmaceutical patents from the novelty requirement, there is a chance that the law could be challenged by a country with a substantial stake in the generic-drug industry, such as India or Israel. *See* Shimon Amselem, *The Biopharmaceutical Industry in Israel*, BUSINESS BRIEFING: PHARMATECH 2002, *at* http://www.touchbriefing.com/pdf/17/pt031_r_2_amselem.pdf; William Greene, *The Emergence of India's Pharmaceutical Industry and Implications for the U.S. Generic Drug Market*, U.S. International Trade Commission, Office of Economics, Working Paper No. 2007-05-A (May 2007). However, since the existing industry-specific patent provisions in U.S. law have not yet been attacked, the threat of such a challenge may be limited.

[292] Stuart Benjamin and Arti Rai have argued that the PTO already has authority to adopt regulations allowing it to grant patents on obvious inventions when patents are necessary to promote their development, citing gene therapies as an example of where this might be appropriate. *See* Benjamin & Rai, *supra* note 170, at 308.

in limiting the scope of the patents that issue, preventing firms from asserting monopoly power over too wide an expanse of technology.[293] To prevent overly-aggressive patenting, therefore, Congress would have to carefully tailor the proposed exemptions so that firms could only claim non-novel or obvious drugs in narrow patents. The statute would have to walk a delicate line, however, allowing patent claims on drugs that are strong enough to prevent generic competitors from entering the market,[294] but not so strong as to prevent other pharmaceutical companies from pursuing related lines of research.[295] Other problems might also arise from changing the novelty and non-obviousness requirements, such as pharmaceutical companies using the new provisions to "evergreen" their drug patents by using new patent filings to block generic entry after their original patents expire.[296] Pharmaceutical companies have been very creative in their litigation tactics,[297] and any dramatic alterations to the patentability standards are likely to produce unexpected results.

An additional concern with modifying the novelty and non-obviousness requirements to allow the patenting of undeveloped drugs is that it might be unconstitutional under current Supreme Court precedent. Congress can only use the patent system "[t]o promote the Progress of . . . useful Arts,"[298] and according to the Supreme Court, this rule prevents Congress from "authoriz[ing] the issuance of patents

---

[293] *See* MERGES & DUFFY, *supra* note 65, at 383; Suzanne Scotchmer & Jerry Green, *Novelty and Disclosure in Patent Law*, 21 RAND J. ECON. 131 (1990).
[294] *See* F. M. Scherer, *The Pharmaceutical Industry – Prices and Progress*, 351 N. ENG. J. MED. 927, 927 (2004) ("Drug patents provide particularly strong protection against competition from other companies because even a slightly different molecular variant must undergo the full panoply of clinical tests required by the FDA.").
[295] One possible approach to this crafting such a statute would be to tie the exemptions for non-novel and obvious drugs to the FDA regulations governing the approval of generic products and the definition of a "bioequivalent" drug. 21 U.S.C. § 355(j)(8)(B).
[296] *See* Derzko, *supra* note 115.
[297] *See* Eisenberg, *supra* note 115, at 348-49.
[298] U.S. CONST. art. I, § 8, cl. 8.

whose effects are to remove existent knowledge from the public domain."[299] Since the Court has said the purpose of the novelty and non-obviousness requirements is "to exclude from consideration for patent protection knowledge that is already available to the public,"[300] those two doctrines may be constitutional limitations on Congress's power to authorize the grant of patents. As a result, the courts might strike down a law that permits the patenting of any old or obvious invention, even a law directed toward drugs that are unlikely to reach the public without patent protection.

There are other doctrinal reforms that would partially resolve the problem posed by the novelty requirement without running afoul of the Supreme Court's interpretation of the Patent Clause, such as changing the law to make it harder for drugs to fall into the public domain. One of the most significant problems with the current novelty doctrine is the ease with which it allows seemingly trivial disclosures to anticipate later-filed patents on a drug. This hair-trigger approach to the novelty doctrine is often to blame for the new drugs that fall into the public domain prematurely. If Congress wishes to preserve the patentability of those drugs, it could simply increase the amount of information that must be disclosed about a drug before it is considered not novel. In particular, Congress could amend the novelty requirement to ensure that pharmaceutical patents cannot be anticipated by a prior disclosure unless that disclosure would have been sufficient to support a patent on the drug. This reform would resolve only some of the problems caused by the novelty requirement,[301] however, and none of the problems caused by the

[299] Graham v. John Deere Co., 383 U.S. 1, 6 (1966).
[300] Bonito Boats, Inc. v. Thunder Craft Boats, Inc., 489 U.S. 141, 148 (1989).
[301] For example, many of the drugs disclosed by academic researchers in scientific publications might still be considered not novel under this proposed rule. Moreover, pharmaceutical companies and universities sometimes just make a mistake in their effort to patent a drug, creating a sufficient disclosure of the invention but failing to follow through on their patent application. *See, e.g.*, In re Application of Weichselbaum, 2006 WL 4494416, at *2 (Com'r Pat., May 3, 2006).

non-obviousness standard. Additionally, since the heightened novelty requirement imposed by courts has been useful in blocking certain evergreening strategies, the courts might need to craft other doctrines to block those potentially abusive litigation techniques.[302]

The loss of drugs caused by the current novelty and non-obviousness requirements is a serious problem, and Congress would be justified in reforming the patent laws to ensure that those doctrines no longer deter the development of socially valuable drugs. These reforms would come at a price, however, and the most effective ones might actually be unconstitutional. Modifying the novelty and non-obviousness requirements to avoid the problem of unpatentable drugs is therefore a second-best solution.

B. Direct Government Funding

Rather than relying on patent reforms to promote the development of socially valuable drugs that currently cannot be patented, Congress could finance the development of those drugs itself. This approach would allow generic manufacturers to enter the market immediately after a drug is approved by the FDA, saving consumers from the high prices of patented drugs. Unfortunately, the government lacks the capacity to reliably develop these drugs, since it would be unable to identify most of them or complete their preclinical development, has a history of grossly underfunding clinical research, and usually fails to effectively disseminate knowledge of publicly developed therapies to medical practitioners. Without a dramatic overhaul of the current system for

[302] *See supra* text accompanying notes 114-116.

financing pharmaceutical R&D, therefore, government-funded drug development is not a feasible solution to the problem of unpatentable drugs.

The most intuitively appealing strategy for promoting the development of drugs that cannot be patented under the novelty and non-obviousness requirements is for the government to directly fund the clinical trials needed for their approval by the FDA. Information about the safety and efficacy of drugs is a classic example of a public good.[303] If the government were to produce that information on its own, allowing drug companies to manufacture and sell old or obvious drugs without having to invest in clinical trials, the lack of patent protection would cease to be a problem. Moreover, since these drugs would still be in the public domain, people would have access to them at generic prices right away, shielding them from the hardship caused by the higher prices of patented drugs. In theory, therefore, the public would be best served by a system where the government directly funds the necessary clinical trials on unpatentable drugs, as opposed to relying on the award of monopoly rights to encourage private industry to develop them.

As a practical matter, however, there are a number of reasons why the government is probably incapable of reliably developing and commercializing these drugs. First, in most cases the government would find it difficult to identify the old or obvious drugs to develop.[304] Those drugs may have been disclosed to the public in some sense, but their potential value is often known only to the pharmaceutical companies that chose not to develop them. It is unlikely that those companies would hand over such drugs to the government, especially when it has taken on the role of a competing drug

[303] *Cf.* SHAVELL, *supra* note 10, at 111-13.
[304] There might be a few exceptions, such as an obvious controlled-release version of an existing drug.

developer. Without that assistance, the government would probably find no more than a handful of the old or obvious drugs discarded by industry.[305]

Second, even if the government knew about the unpatentable drugs that private industry discards, those drugs are typically screened out of development during early preclinical research, and the government is poorly equipped to complete that preclinical work. At least two of the three patent screens that pharmaceutical companies run their drugs through occur before they have finished (or even begun) the preclinical development work needed to evaluate and improve their pharmacological properties.[306] This stage of research is not only an essential step in the drug development process,[307] it is also one of the most complicated and difficult of the entire process,[308] and government laboratories are not set up for this work.[309] The human and technological capital necessary for developing a lead compound into a drug ready for clinical trials and wide-scale production is located almost exclusively by the private sector,[310] and neither government nor academia could easily replicate that infrastructure.[311] The government therefore lacks the technological capacity to develop most of the unpatentable drugs that pharmaceutical companies drop from their pipeline.

---

[305] Perhaps the government could offer rewards to private industry for disclosing the unpatentable drugs that they would have developed but for the absence of patent protection. Establishing such a reward system would be complicated, however, because the government would need a reliable way of linking its reward to the actual value of the drug. If such a reward system were ever devised, it is unclear why its use would be limited to unpatentable drugs.

[306] *See supra* text accompanying notes 222-227.

[307] *See* MacCoss & Baillie, *supra* note 224.

[308] *See* Galli & Faller, *supra* note 188, at 689; MacCoss & Baillie, *supra* note 224, at __.

[309] "Academic and government laboratories . . . are rarely organized . . . to embrace the drug discovery process in the multidisciplinary fashion . . . that is the modern paradigm by which new hits or leads are . . . transformed into new viable medicines." MacCoss & Baillie, *supra* note 188, at __.

[310] Martina Casenghi et al., *New Approaches to Filling the Gap in Tuberculosis Drug Discovery*, PLOS MED., vol. 4, Nov. 2007, at 1; John S. Lazo, *Roadmap or Roadkill: A Pharmacologist's Analysis of the NIH Molecular Libraries Initiative*, 6 MOLECULAR INTERVENTIONS 240, 241 (2006).

[311] *See* Casenghi et al., *supra* note 309, at 3.

Third, it is doubtful Congress would allocate sufficient funds for the development of unpatentable drugs. Although the potential benefits from government financing of clinical research are substantial,[312] funding for government-sponsored clinical trials is chronically in short supply,[313] and recent spending cuts reflect Congress's unwillingness to commit necessary resources to important clinical research.[314] Private industry likely under-invests in clinical trials as well, since the social costs of clinical trials are much lower than their private costs – which include the entire costs of medical care for study participants even though most of them would otherwise be receiving alternative medical treatments paid for by their insurer[315] – and monopoly profits from the sale of patented drugs are lower than their social value.[316] Nevertheless, the public still relies on private industry to finance the bulk of clinical research.[317] If Congress were to be tasked with paying for the development of non-novel or obvious drugs, there is little reason to believe the funding would be adequate.

Fourth, assuming that the government funds clinical trials on unpatentable drugs and establishes their safety and efficacy, that research can fall on deaf ears without

---

[312] *See* S. Claiborne Johnston et al., *Effect of a US National Institutes of Health Programme of Clinical Trials on Public Health and Costs*, 367 LANCET 1319 (2006).

[313] *See* Jennifer Couzin, *Tight Budget Takes a Toll on U.S.-Funded Clinical Trials*, 315 SCIENCE 1202, 1202-03 (2007); Mike Mitka, *Scientists Warn NIH Funding Squeeze Hampering Biomedical Research*, 297 JAMA 1867, 1867 (2007); Charlie Schmidt, *Public vs. Private: Cooperative Groups Say NCI Trials Funding Inadequate; Some Turn to Industry*, 99 J. NAT'L CANCER INST. 830, 830-32 (2007); Nancy S. Sung, *Central Challenges Facing the National Clinical Research Enterprise*, 289 JAMA 1278, 1284-85 (2003).

[314] *See* Joseph Loscalzo, *The NIH Budget and the Future of Biomedical Research*, 354 NEW ENG. J. MED. 1665, 1665-66 (2006); Mitka, *supra* note 313, at 1867 (noting that between 2003 and 2007, NIH funding fell by 16 percent when adjusted for inflation).

[315] *See* Charles L. Bennett et al., *Clinical Trials: Are They a Good Buy?*, 19 J. CLINICAL ONCOLOGY 4330 (2001); Dana P. Goldman et al., *Incremental Treatment Costs in National Cancer Institute-Sponsored Clinical Trials*, 289 JAMA 2970, 2974-75, 2976 (2003) (finding that in government-funded clinical trials for cancer research, the total cost of the trials is only 6.5% higher than the cost of care those patients would have received outside of the trials).

[316] *See* Shavell & Ypersele, *supra* note 34, at 529.

[317] *See* Hamilton Moses et al., *Financial Anatomy of Biomedical Research*, 294 J. AM. MED. ASS'N 1333 (2005).

private industry to promote it. Unlike pharmaceutical companies, who aggressively market their products, the government is often content with publishing research outcomes in medical journals,[318] which can have a limited impact on physician practices.[319] The government-funded clinical trial on the use of finasteride for cancer prevention, described in Part III above, appears to be an example of where the government's failure to market a potentially life-saving drug is delaying (or perhaps preventing) its widespread use.[320] There are likely other examples as well, including the slow pace at which the medical profession adopted antibiotics as a treatment for ulcers.[321] Although pharmaceutical

[318] *See* AVORN, *supra* note 113, at 292-94.
[319] *See supra* note 272.
[320] *See supra* text accompanying notes 264-275. The government-funded clinical trials on tamoxifen for preventing breast cancer *might* be another example. *Cf.* Liz Savage, *Researchers Wonder Why High-Risk Women Are Not Taking Chemoprevention Drugs*, 99 J. NAT'L CANCER INST. 913, 913-14 (2007).
[321] Researchers first discovered that most peptic ulcers could be cured with antibiotics in 1982, but because those antibiotics were off-patent, the researchers found it difficult to find a sponsor for testing the treatment in clinical trials. *See* Marshall, *supra* note 106, at 199. After a few years the researchers were able to run a number of studies and confirm the effectiveness of the antibiotic treatment. *Id*. at 187-201. Nonetheless, the pharmaceutical companies holding patents on acid-reducing drugs "effectively drowned out much of the[ir] research by funding hundreds of acid reduction trials." *Id*. at 199. Even after the NIH issued a consensus statement in 1994, a decade later, stating that ulcers should be treated with a combination of antibiotics and acid-reducing drugs, *see* NIH Consensus Development Panel, *supra* note 106, at 67-68, most primary-care physicians in the United States were slow to adopt the new treatment, largely due to a lack of awareness of its effectiveness. *See* Thomas Breuer et al., *How Do Clinicians Practicing in the U.S. Manage Helicobacter pylori-Related Gastroinestinal Diseases? A Comparison of Primary Care and Specialist Physicians*, 93 AM. J. GASTROENTEROLOGY 553 (1998). In the practice of medicine, "[p]harmaceutical marketing is the most important source of knowledge about new drugs for most physicians," AVORN, *supra* note 113, at 292, and up until 1996, when the manufacturer of Prilosec® secured FDA approval for the Prilosec®-antibiotic combination as a treatment for ulcers, there was no one to market the NIH-recommended treatment to physicians. *See H. Pylori Treatment Recognized by FDA*, 53 AM. J. HEALTH-SYS. PHARMACY 1229, 1229 (1996); MAE THAMER ET AL., PHYSICIAN PRESCRIBING AMONG PRIVATELY INSURED PEPTIC ULCER DISEASE PATIENTS 16-17 (1999), *at* http://www.mtppi.org/pdfs/pud_paper.pdf. It was not until the late 1990s that most physicians were treating ulcer patients in a manner consistent with NIH recommendations. *See* Roger J. Zoorob et al., *Practice Patterns for Peptic Ulcer Disease: Are Family Physicians Testing for H. Pylori?*, 4 HELICOBACTER 243, 246-47 (1999); V.K. Sharma & C.W. Howden, *A National Survey of Primary Care Physicians' Perceptions and Practices Related to Helicobacter Pylori Infection*, 4 J. CLINICAL GASTROENTEROLOGY 326 (2004). It is likely that this change is at least partially attributable to the marketing efforts behind Prilosec®. *See* H. J. O'Connor, *Helicobacter Pylori and Dyspepsia: Physicians' Attitudes, Clinical Practice, and Prescribing Habits*, 16 AILMENT PHARMACOLOGY & THERAPEUTICS 487, 493 (2001).

marketing can be noxious,[322] the failure to promote a valuable new drug can be just as bad when it prevents that drug from being used.[323]

For these reasons, and perhaps others, the government is ill-suited to the task of developing and commercializing unpatentable drugs. This is not to say that the government could never play a more direct role in the financing of drug development. It is possible that Congress could implement elaborate reforms to overcome the problems with government funding identified above, such as instituting some sort of payment or reward system to encourage private industry to develop drugs that cannot be patented. If such a system were to be created, however, it is unclear why it should be limited to only unpatentable drugs, rather than attempting to eliminate the deadweight loss caused by drug patents more generally. These types of policy proposals are beyond the scope of this paper.

C. FDA-Administered Exclusivity Periods

In the end, the best way for Congress to promote the development of unpatentable drugs is through the FDA, requiring the agency to withhold regulatory approval from generics for long enough to replicate the protection normally provided by patents. These FDA-administered exclusivity periods can fill the gaps left by the novelty and non-obviousness requirements by guaranteeing an adequate period of market exclusivity to any drug that successfully completes the FDA's clinical trial requirements. Congress could implement this proposal with only modest changes to existing law, since the FDA

[322] *See generally* ANGELL, *supra* note 180, at 115-72; JOHN ABRAMSON, OVERDOSED AMERICA: THE BROKEN PROMISE OF AMERICAN MEDICINE (2004).

[323] This problem might be most severe when a non-novel or obvious drug developed by the government must compete against patented drugs being marketed by pharmaceutical companies.

is already required to impose short delays on generic manufacturers. Solving the problem of unpatentable drugs simply requires lengthening those existing regulatory delays. Moreover, since the FDA's regulatory requirements are themselves what drive much of the need for protection in the pharmaceutical industry, linking the reward of exclusivity to successfully completing clinical trials is a sensible approach to promoting innovation.

While pharmaceutical companies currently rely on the market exclusivity afforded by patents to recoup their R&D investments, Congress could use the FDA to provide roughly the same level of protection. Generic drugs cannot be sold to the public without FDA approval, and Congress can build automatic delays into that process – lasting ten or more years – to mimic the effects of strong patent protection.[324] A lengthy exclusivity period administered by the FDA should provide nearly the same inducement for pharmaceutical innovation as do patents, and therefore solve the problems created by the novelty and non-obviousness requirements. [325]

Fortunately, the basic framework for these FDA-administered exclusivity periods is presently in place;[326] Congress just needs to lengthen certain regulatory delays that already exist under current law. When Congress first authorized abbreviated regulatory review for generic drugs in 1984,[327] exempting generics from the FDA's clinical trial

[324] Since these FDA-administered periods of exclusivity are essentially trade secrecy provisions protecting the clinical trial data submitted by pharmaceutical companies, and do not guarantee market exclusivity, *see infra* note 329, they probably would not be subject to any possible constitutional limitations on Congress' patent power.

[325] *See* Valerie Junod, *Drug Marketing Exclusivity Under United States and European Union Law*, 59 FOOD & DRUG L.J. 479, 484-85 (2004) (noting that marketing-exclusivity periods can encourage the development of unpatentable drugs).

[326] *See* Eisenberg, *supra* note 115, at 359-61.

[327] *See* Drug Price Competition and Patent Term Restoration (Hatch-Waxman) Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (codified as amended in scattered sections of the U.S.C.).

requirements,[328] it required the FDA to wait between five and seven and one-half years after approving most new drugs before allowing generics onto the market.[329] It is unclear whether these regulatory delays were designed to encourage the R&D of unpatentable drugs,[330] or, more likely, to simply coordinate the timing of patent challenges by generic drug manufacturers.[331] In either case, there is compelling evidence that the current

[328] The FDA will approve a generic drug without clinical-trial evidence of its safety and efficacy if the generic is "bioequivalent" to a drug that the FDA already approved. *See* 21 U.S.C. § 355(j)(8)(B).

[329] The duration of FDA-enforced exclusivity depends on the drug at issue. If a new drug contains an active ingredient that was previously approved by the FDA, then it receives only three years of data exclusivity. 21 U.S.C. § 355(c)(3)(E)(iii). During that three-year period, the FDA will not approve generic versions of the drug in its new form or labeled for its new use unless the generic applicant relies upon its own clinical-trial data in support of the application. *See id*. If a new drug does not contain any previously-approved active ingredients, then it is known as a new molecular entity ("NME"), and it receives five years of data exclusivity. *Id*. at § 355(c)(3)(E)(ii). For NMEs, the effective duration of that five-year period varies depending upon whether it is patented. When an NME is patented, and the patent holder files an infringement lawsuit against the generic competitors trying to enter the market, the FDA typically withholds its approval of the generic product for seven and one-half years following the NME's initial approval. *See id*. When the NME is not patented, the FDA begins to accept applications for generics as soon as the five-year period expires, *see id*., and since it takes them an average of 16 months to approve an application for a generic drug, *see* Steven K. Galson, *2006 CDER Update* 11, (Jan. 18, 2007), *at* http://www.fda.gov/cder/present/galson/default.htm, the five years of exclusivity usually amounts to six and one-third years. In each of these cases, generic companies can bypass the FDA-enforced exclusivity periods by submitting their own clinical-trial data. The only exception is for "orphan" drugs, which receive a different form of protection. 21 U.S.C. § 360cc(a); *see supra* note 258.

[330] These regulatory delays may have been designed to encourage the development of unpatentable drugs, *see* H.R. REP. NO. 98-857, at 29 (1984), although scholars and policymakers have (until now) been unable to identify categories of unpatentable drugs that would justify the delays, *see, e.g.*, Junod, *supra* note 325, at 484-85, and it was widely assumed that any drug that fails to satisfy the patentability requirements deserves little or no protection. *See* John Thomas, *Proprietary Rights in Pharmaceutical Innovation: Issues at the Intersection of Patents and Marketing Exclusivities*, CRS REPORT FOR CONGRESS, at CRS-13-14 (2006).

[331] The existing FDA-administered exclusivity periods may serve primarily the interests of generic manufacturers. The Hatch-Waxman Act rewards the first generic company to successfully challenge a drug patent with 180 days of being the only (unauthorized) generic on the market. *See* 21 U.S.C. § 355(j)(5)(B)(iv). This bounty system creates a race among generic companies to be the first to file a patent challenge. Absent the 5-year exclusivity period provided in the Hatch-Waxman Act, competition among generic companies would force them to file their challenges as early as possible. The successful companies would likely be launching their generic products just a few years after the original drug first entered the market. Sales of most blockbuster drugs do not take off until after their fourth or fifth years, however, usually after substantial marketing efforts. *See* Henry Grabowski et al., *supra* note 167, at 17-18. Consequently, the market-exclusivity provisions in the Hatch-Waxman Act force generic companies to delay their patent challenges in a way that likely increases their industry's profits. *Cf.* Alfred B. Engelberg, *Special Patent Provisions for Pharmaceuticals: Have they Outlived Their Usefulness? A Political, Legislative and Legal History of U.S. Law and Observations for the Future*, 39 IDEA 389, 406 (1999) (explaining that the five-year exclusivity periods in Hatch-Waxman "did not deprive [generic manufacturers] of any important economic right since there is no real incentive to develop a generic drug until a market has been established . . .").

periods of FDA-administered exclusivity are inadequate,[332] since pharmaceutical companies continue to screen drugs with weak patent protection out of their pipeline.[333] If the existing market-exclusivity periods were long enough to make unpatentable drugs a profitable investment, then private industry should already be developing them, even if the expected profit is less than what firms would receive from a patented drug.[334] Consequently, although it is difficult to calculate the precise optimal length of exclusivity for drugs,[335] there is a very high probability that the optimal length is longer than the current five to seven and one-half years. By lengthening that period to somewhere between ten and fourteen years, Congress would at least provide a rough substitute for patent protection,[336] and thus eliminate the distortions arising from the novelty and non-obviousness requirements.[337]

Compared to patents, these FDA-administered exclusivity periods are a more sensible tool for promoting the development of unpatentable drugs, since the reward of exclusivity is given in exchange for satisfying the FDA's regulatory requirements, and

---

[332] *See* Grabowski, *supra* note 331, at 21 ("Only drugs with sales revenues in the top decile of new introductions would generally earn enough to recoup the mean R&D investment within 7 years."). According to several industry executives interviewed for this article, the FDA-enforced periods of market exclusivity are generally insufficient to justify the expense of developing and commercializing a new drug. *See* Telephone Interview with Anonymous, Director of Intellectual Property, *supra* note 228 (explaining that the FDA-enforced exclusivity periods alone are rarely sufficient for a pharmaceutical company to move forward on a drug project); Telephone Interview with Anonymous, Senior Intellectual Property Counsel, *supra* note 230 (stating that seven years of exclusivity is sometimes sufficient, although most often it is not); *cf.* Telephone Interview with Declan Doogan, *supra* note 251 (explaining that the 7 years of market exclusivity for orphan drugs is only occasionally sufficient for firms to develop them).

[333] *See supra* text accompanying notes 222-251.

[334] *See supra* text accompanying notes 254-255. Under some circumstances firms might discard unpatentable drugs even if the current 5 to 7½ years of exclusivity is adequate for them to recoup their R&D investment; *e.g.*, if the industry is facing severe, long-term resource constraints (perhaps a skilled-labor shortage) that forces firms to invest in only the most profitable drugs available. *See supra* note 255.

[335] *See* Louis Kaplow, *The Patent-Antitrust Intersection: A Reappraisal*, 97 HARV. L. REV. 1813, 1823-39 (1984).

[336] *See supra* note 289.

[337] Generics typically do not enter the market until 10 to 14 years after the initial launch of the name-brand drug. *See* Grabowski & Kyle, *supra* note 28; Grabowski & Vernon, *supra* note 28, at 109-117; Scherer, *supra* note 294, at 927.

those requirements are the primary reason why exclusivity is necessary. The FDA requires new drugs to be proven safe and effective in clinical trials before they can be marketed, which involves tremendous cost and risk. At the same time, the FDA permits generic competitors to enter the market without satisfying those regulatory requirements, allowing them to free-ride upon the pharmaceutical companies' investments in clinical trials. Whenever the FDA requires that a drug be proven safe and effective in clinical trials before entering the market, therefore, some guarantee of market exclusivity is likely necessary to encourage its development.[338] Conversely, if a non-novel or obvious drug can enter the market without extensive clinical-trial testing, then this lengthy award of exclusivity may be unnecessary. FDA-administered exclusivity periods link the promise of market exclusivity with the need for that protection, and are therefore a logical approach to promoting investment in clinical trials.

Other adjustments to these FDA-administered periods of market exclusivity might further improve the incentives for pharmaceutical innovation. The duration of exclusivity awarded under a regulatory regime – as opposed to the less flexible patent system – could be tailored in accordance with the varying R&D costs and risks of different drugs. In fact, since the exclusivity periods would be awarded in exchange for satisfying the FDA's regulatory requirements, and those regulatory requirements are the primary reason why drug development is so costly, the FDA is in a unique position to link the duration of market exclusivity to the burden of meeting its own requirements. Longer and more expensive clinical trials likely require more protection, whereas shorter and cheaper trials

[338] *See supra* text accompanying notes 21-30.

could be motivated with a briefer period of exclusivity.[339] Additionally, the FDA could discourage the development of "me too" drugs by withholding the market-exclusivity rewards – or even regulatory approval – from new drugs until there is clinical-trial evidence documenting their therapeutic advantages over older drugs.[340] It is unclear whether such a policy would benefit the public,[341] but it certainly makes more sense to use the FDA for this task than the PTO, which has neither the institutional expertise nor the experimental data necessary for making these judgments soundly.[342]

The only significant problem with the FDA-enforced exclusivity periods is that they might permit wasteful development races in clinical research, but this problem can be avoided. If no single firm is given the exclusive rights to develop a drug, multiple competing firms could decide to run clinical trials on it at the same time in the hopes of being the first to receive FDA approval. The FDA could easily prevent such races, however, since firms cannot begin testing a drug in clinical trials without the FDA's approval,[343] and it could give its approval to only one firm.[344] So long as the FDA guards against these development races, its ability to block entry by generic competitors is the most promising strategy for avoiding the harm now caused by the novelty and non-obviousness requirements.

---

[339] Interestingly, the patent system currently does the exact opposite. The 20-year patent term runs from the date when the patent is filed, which occurs during early preclinical research for most drugs. As a result, the longer a drug is in development, the shorter its effective patent life becomes, even though the need for protection is likely greater.

[340] *See* ANGELL, *supra* note 180, at 240-42; *but see* AVORN, *supra* note 113, at 365.

[341] *See supra* note 192.

[342] *See supra* text accompanying notes 184-192.

[343] *See* 21 U.S.C. § 505(i).

[344] In the event that the initial firm fails to develop the drug, the FDA could allow another one to begin testing it.

CONCLUSION

The record of innovation in the pharmaceutical industry is one of the patent system's crowning achievements, and it can probably take credit for much of the $55.2 billion spent by private industry on pharmaceutical R&D last year alone.[345] Nonetheless, there remains considerable room for improvement in the system. While many commentators extol the virtues of pharmaceutical patents in promoting innovation,[346] and other scholars criticize those patents for providing too much protection over drugs,[347] they have all overlooked how the patent system often fails to provide *any* protection to valuable drugs. These unpatentable drugs are generally ignored by private industry, and as a result, they rarely reach the public.

This stunning failure in innovation policy is caused by the patent system's novelty and non-obviousness requirements, which have been crafted under the flawed assumption that patents are only needed to promote the creation of inventions, not their development or commercialization. Under current law, once the idea for a drug has been disclosed to the public or becomes obvious, that drug is no longer patentable. Without private industry to develop that idea into an FDA-approved drug, however, the public is unlikely to ever benefit from its use. Since pharmaceutical companies rarely invest in drugs without patent protection, the novelty and non-obviousness requirements take on a pernicious role in the industry: seemingly trivial disclosures of drugs often prevent those drugs from later being patented and developed; the drugs that appear most likely to be

---

[345] *See* Press Release, Pharmaceutical Research and Manufacturers of America (PhRMA), *R&D Spending by U.S. Biopharmaceutical Companies Reaches a Record $55.2 Billion in 2006*, at http://www.phrma.org/news_room/press_releases/r%26d_spending_by_u.s._biopharmaceutical_companies_reaches_a_record_%2455.2_billion_in_2006/.

[346] *See supra* notes 1, 2.

[347] *See, e.g.*, Engelberg, *supra* note 331; Mark A. Lemley & Kimberly A. Moore, *Ending Abuse of Patent Continuations*, 84 B.U. L. REV. 63, 82-84 (2004).

effective in early research are singled out as being obvious, and are thus discarded by private industry; and the scientific advances that allow researchers to more easily identify promising drug candidates become the basis for withholding patent protection from those drugs.

These ill-conceived doctrines have a direct and negative impact on the investment decisions made by private industry, causing pharmaceutical companies to screen otherwise promising drugs out of development due to perceived inadequacies in their patent protection. The public rarely learns of these drugs, of course, because they are seldom developed for medical use. The detrimental consequences of the novelty and non-obviousness requirements thus remain mostly hidden from public view. In light of the tremendous benefits that pharmaceuticals often provide to society, however, there is great cause for concern. Congress should prevent these harms by modifying FDA regulations to ensure that newly-approved drugs receive adequate protection in the form of automatic regulatory delays imposed upon generic competitors.