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DISTORTED DRUG PATENTS

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DISTORTED DRUG PATENTS

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Drug patents are distorted. Unlike most other inventors, drug inventors must complete years of testing to the government's specifications and seek government approval to commercialize their inventions. All the while, the patent term runs. When a drug inventor finally launches a medicine that embodies the invention, only a fraction of the patent life remains. And yet, conventional wisdom holds — and empirical studies show — that patent life is essential to innovation in the pharmaceutical industry, perhaps more so than any other inventive industry. Congress tried to do something about this in 1984, authorizing the Patent and Trademark Office to “restore” a portion of the patent lost to premarket testing. PTO doesn't restore all of the lost time, though, which raises the question whether the U.S. legal system may steer researchers away from drugs that take a long time to develop. This Article focuses on that question. It examines every grant of patent term

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restoration for a new drug or biologic from the scheme's 1984 enactment to April 1, 2018. And it fills a conspicuous gap in the literature: few scholars have considered patent term restoration from an empirical perspective, none has used a dataset of this size and scope, and none has addressed the questions this Article addresses. Two significant conclusions stand out. First, longer clinical programs lead to shorter effective patent life, even after PTO has granted patent term restoration. The results are strongly statistically significant and contribute to a growing body of literature raising the alarm that the U.S. legal system may be systematically skewing drug research incentives away from the harder problems — such as a cure for Alzheimer's Disease and interventions at the early stages of cancers. Second, Congress decided to allow drug companies to apply patent term restoration to continuation patents, specifically because this would increase the chances of reaching 14 years of effective patent life. Ten years later Congress changed the way patent terms are calculated without considering the effect on patent term restoration. Selecting a continuation patent no longer has the same effect. Today a drug company is most likely to achieve the 14 years of effective patent life by securing a new, original patent that issues late in clinical trials. Policymakers and scholars complain when companies secure these later-expiring patents, but the findings in this Article suggest those patents may be necessary to accomplish what Congress intended in 1984.

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INTRODUCTION

New medicines are famously expensive and can remain so for years, until copies become available. Concern about their prices and the wait for cheaper copies has sparked legislative hearings and policy proposals over the years — including, recently, suggestions that the government impose price controls or even strip drug companies of their patent rights.¹ These proposals implicate another significant public policy challenge: that we still lack effective treatments for many serious diseases. We have no meaningful treatment for Alzheimer’s Disease, for instance, even though ten percent of the U.S. population aged 65 or older has been diagnosed with Alzheimer’s dementia, and the number of sufferers is projected to reach 7.1 million by 2025.² And many cancers — such as pancreatic cancer, diffuse intrinsic pontine glioma, and glioblastoma multiforme — remain essentially untreatable.³ Many chronic diseases, though treated, continue to exact a toll. Ten years ago researchers at the Milken Institute estimated that seven chronic diseases — cancer, heart disease, hypertension, mental disorders, diabetes, pulmonary conditions, and stroke — together affect more than 109 million Americans, with a total impact on the economy of \$1.3 trillion annually.⁴ According to the RAND Corporation, 60 percent of Americans have at least one chronic condition, and 42 percent have multiple chronic conditions.⁵ The health care costs associated with chronic diseases accounted for 86 percent of the nation’s \$2.7 trillion annual health care expenditures in 2014.⁶ Better

¹ E.g., Robin Feldman, *May Your Drug Price be Evergreen*, 7 J. LAW BIOSCI. 590 (2018) (proposing that drug companies be limited to one patent or period of exclusivity); Hannah Brennan et al., *A Prescription for Excessive Drug Pricing: Leveraging Government Patent Use for Health*, 18 YALE J. L. & TECH. 275 (2016) (arguing that the U.S. government should invoke 28 U.S.C. § 1498 to authorize generic manufactures to produce patented drugs, without permission of the patent owner, subject to “reasonable compensation”); S. 1416 (116th Cong.) (introduced May 9, 2019) (proposing to presume it an “unfair method of competition in or affecting commerce” to obtain certain additional later-expiring patents in the same patent family or portfolio as an already issued patent that claims an approved drug).

² Alzheimer’s Association, *2018 Alzheimer’s Disease Facts and Figures*, 14 ALZ. DEMENTIA 367 (2018).

³ E.g., Ho-Shin Gwak & Hyeon Jin Park, *Developing Chemotherapy for Diffuse Pontine Intrinsic Gliomas (DIPG)*, 120 CRIT. REV. 111 (2017) (noting median survival rate of 10 months after radiation).

⁴ Ross DeVol & Armen Bedroussian, *AN UNHEALTHY AMERICA: THE ECONOMIC BURDEN OF CHRONIC DISEASE* (2007).

⁵ Christine Buttorff, et al., *MULTIPLE CHRONIC CONDITIONS IN THE UNITED STATES*, RAND Corporation (2017).

⁶ Aspen Health Strategy Group, *REDUCING THE BURDEN OF CHRONIC DISEASE* (2019).

treatments for these conditions are needed.

The two issues — the high price of new medicines, and the need for new medicines — are intertwined. The U.S. legal system stimulates the invention and development of new medicines in part by promising a period of exclusivity in the market, which is attractive *because* it provides an opportunity to charge higher prices during the period.⁷ This exclusivity is made possible in part by the protection of patents associated with those new medicines.⁸ Patent protection ensures that an inventor can enjoy a period during which others cannot make or sell copies of the invention.⁹ The patent

⁷ Edmund W. Kitch, *The Nature and Function of the Patent System*, 20 J. L. & ECON. 265 (1977); see also Benjamin N. Roin, *Unpatentable Drugs and the Standards of Patentability*, 87 TEX. L. REV. 503, 508 (2009) (“Without some way to delay generic competition ... 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 drugs, providing them an opportunity to profit from their investment in R&D.”).

⁸ It is also made possible in part by the “data exclusivity” provisions of the two drug approval statutes. During the data exclusivity period, other companies may not rely in their own applications on the research generated and submitted by an inventor to support approval of its drug. *E.g.*, 21 U.S.C. § 355(j)(5)(F)(ii) (providing that generic applications cannot be submitted until five years after approval of a new drug with a new active ingredient, or four years in the case of a patent challenge).

There may be other ways to stimulate the invention and development of new medicines. *E.g.*, Michael Abramowicz, *Perfecting Patent Prizes*, 56 VAND. L. REV. 115 (2003) (assessing a variety of proposed “prize” systems in which the government pays monetary compensation and recommending a “flexible, retrospective” system administered by an administrative agency); Michael R. Kremer, *Patent Buy-Outs: A Mechanism for Encouraging Innovation*, 113 QUAT. J. ECON. 1137 (1998) (considering a mechanism in which the government offers to purchase patents at their private value, determined using an action, adjusted by a markup to cover the difference between the patent’s social value and its private value); Aidan Hollis, *An Efficient Reward System for Pharmaceutical Innovation*, UNIVERSITY OF CALGARY WORKING PAPER (June 2004) (proposing a system in which innovators are rewarded by direct payment from a government-financed fund based on the “incremental therapeutic benefits” of their innovation); Kristina M. Lybecker & Robert A. Freeman, *Funding Pharmaceutical Innovation through Direct Tax Credits*, 2 HEALTH ECON., POL’Y & LAW 267 (2007) (proposing as an alternative to the current patent system an approach of rewarding innovators with direct tax credits in exchange for marginal cost pricing); James Love & Tim Hubbard, *The Big Idea: Prizes to Stimulate R&D for New Medicines*, 82 CHI.-KENT L. REV. 1519 (2007) (recommending that the government award innovators with large prizes tied to the actual impact of the medicine on healthcare outcomes); Rachel E. Sachs, *Prizing Insurance: Prescription Drug Insurance as Innovation Incentive*, 30 HARV. J. L. & TECH. 153 (2016) (proposing a change to the government health insurance program for low-income individuals, Medicaid, to reward innovators who bring to market drugs for diseases primarily affecting low-income populations).

⁹ See generally *infra* section I.B. There is debate in the literature about whether patents promote not only invention (discovery) but also post-invention development efforts. Compare Kitch, *supra* note 7 (arguing that early-issued patents give their owners “an incentive to make investments to maximize the value of the patent”) with Mark A. Lemley,

thus encourages innovation, because it, by design, permits a temporary high price for the resulting new medicine.¹⁰ Although there is disagreement on the matter, many conclude that we cannot have the one (the innovation) (medicine) without the other (the encouragement to innovate) (a temporarily high price).¹¹ What remains is the question of balancing: how much exclusivity in the market is needed for the optimal amount of medical innovation.¹²

Ex Ante Versus Ex Post Justifications for Intellectual Property, 71 U. CHI. L. REV. 129 (2004) (disputing Kitch’s “prospect theory” and notion “that a single company is better positioned than the market to make efficient use of an idea”). This debate does not affect the point made in the text. The point is that without the promise of a period of exclusivity in the market, the prospect of competition will deter investment in the post-invention research and development needed to commercialize a new medicine.

¹⁰ Patent protection for new drugs has its limitations, however. See Rebecca S. Eisenberg, *The Shifting Functional Balance of Patents and Drug Regulation*, 20 HEALTH AFFAIRS 119 (2001) (pointing out shortcomings of patent-based exclusivity for new drugs, including the possibility of patents held by third parties for prior discoveries that may be essential to development of the drug in question and increasing public hostility to patents due to rising health care costs); Yaniv Heled, *Why Primary Patents Covering Biologics Should Be Unenforceable Against Generic Applicants Under the Biologics Price Competition and Innovation Act*, 21 ANNALS HEALTH L. 211 (2012) (suggesting that patents for biologics products are vulnerable to workarounds).

¹¹ E.g., Roin, *Unpatentable Drugs*, *supra* note 7, at 508 (“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.”); see also Kristina M.L. Aciri, *Economic Growth and Prosperity Stems from Effective Intellectual Property Rights*, 24 GEO. MASON L. REV. 865, 868 (2017) (“Without patent protection, and other forms of intellectual property rights to protect an innovator’s investment, pharmaceutical drug development will not take place.”); F.M. Scherer, *The Pharmaceutical Industry – Prices and Progress*, 351 THE NEW ENGLAND JOURNAL OF MEDICINE 927 (2004) (“Numerous cross-industry surveys have shown that managers of pharmaceutical research and development assign unusually great importance to patent protection as a means of recouping their investment in research, development, and testing.”).

¹² There is extensive theoretical literature analyzing optimal patent term, dating to Professor Nordhaus’s seminal work in 1969, with which this Article does not engage. William Nordhaus, *INVENTION, GROWTH, AND WELFARE: A THEORETICAL TREATMENT OF TECHNOLOGICAL CHANGE* (1969) (proposing that optimal patent length balances the tradeoff between eliciting activity that would not otherwise have occurred, on the one hand, and giving monopoly protection to inventions that would have been shared with society anyway, on the other hand). There is less empirical literature on the subject. See Eric Budish et al., *Patents and Research Investments: Assessing the Empirical Evidence*, 106 AM. ECON. REV. 183 (2016) (reviewing the “surprisingly small body of empirical evidence” assessing the elasticity of investment with respect to patent term length). Recently, however, some have argued that patent term should be tailored to field of invention or to time to market. E.g., Eric Budish et al., *Do Fixed Patent Terms Distort Innovation? Evidence from Cancer Clinical Trials*, SIEPR Discussion Paper No. 13-001 (Sept. 5, 2013) ([here](#)) (suggesting that with fixed patent terms, research and development is “distorted away from technologies with

This Article focuses on the relationship between the patent incentive and drug innovation, adding an empirical dimension relating to the length of drug patents that has been lacking in the scholarship to date. It focuses on the fact that the patent incentive does not work the same way for medicines as it does for other inventions — because a separate body of federal law *bans* the inventor from marketing the invention for sometimes half — or even more — of the patent life. That is, federal regulatory requirements “distort” the patent.¹³

Since the early 20th century, federal law has required the sellers of medicines to test their products and seek the government’s permission before launching.¹⁴ A new medicine must be proven safe and effective for a particular medical use.¹⁵ Satisfying this standard entails laboratory and animal (“preclinical”) testing as well as several phases of human (“clinical”) trials. The federal government’s gatekeeping mechanism protects public health by ensuring that new medicines are, on average, more beneficial than harmful for the patients for whom they are intended.¹⁶ But gatekeeping comes at a price: the research required by the U.S. Food and Drug Administration (FDA) is not only expensive and time consuming, but risky.¹⁷ The inventor must make an enormous investment, without knowing whether the medicine will succeed in trials (or for what, exactly), without knowing when the trials will be completed and the medicine approved, and without knowing whether (if approved) the medicine will be commercially successful.¹⁸

Distortion of the patent term stems from the fact that medicine inventors usually file their first patent applications *before* they start testing in humans.¹⁹ This generally means that the patents issue *before* the trials are done and before approval of the medicine. And while the premarket testing continues, the patent life runs. By the time the federal government permits the inventor to commercialize the invention, much of the patent term has lapsed. The years that remain are the “effective” life of the patent — the years during

long time lags between invention and commercialization”); Benjamin N. Roin, *The Case for Tailoring Patent Awards Based on the Time-to-Market*, 61 UCLA L. REV. 672 (2014) (arguing that time to market is a “uniquely powerful indicator of the optimal patent strength for different types of inventions”).

¹³ *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 669 (1990).

¹⁴ See generally *infra* section I.A.

¹⁵ See *id.*

¹⁶ Patricia J. Zettler, *Pharmaceutical Federalism*, 92 IND. L. J. 845, 857 (2017); see also Erika Lietzan, *Access Before Evidence and the Price of the FDA’s New Drug Authorities*, 53 U. RICH. L. REV. 101, 136-45 (2019).

¹⁷ See *infra* section I.A.

¹⁸ See *infra* section I.A. and note 54.

¹⁹ See *infra* section I.B.

which the inventor may lawfully exploit the invention in the market, without others also using the invention. The irony for inventors of new medicines is that medicines requiring *more* premarket investment (more years of research) may enjoy *less* patent life at the end of the day.

The problem grew worse in the 1960s and 1970s as the federal regulatory framework grew more demanding.²⁰ In 1984, Congress responded to this fact, and to data showing a decline in drug innovation, with an amendment to the Patent Act.²¹ As a result the U.S. Patent and Trademark Office (PTO) now restores a portion of the drug patent term lost to premarket research and development and FDA review.²² But it does not restore all of the time lost. It restores only half of the clinical testing time (after the patent issues), and it caps the recovery at five years, no matter how long clinical trials and FDA approval take. This means that after a certain point, premarket research and development simply translates into lost patent life. The statute also limits the patent to fourteen years of life after drug approval, meaning that the restored patent may not expire later than the fourteen-year anniversary of FDA's approval of the drug.

As a regulatory matter, the length of a drug's premarket clinical program mostly reflects factors outside the control of the company developing the drug.²³ Moreover, some types of drugs consistently take longer in premarket research and development.²⁴ These findings raise the question whether — given the patent term restoration formula — the U.S. legal system systematically under-encourages particular areas of medical research.²⁵

This Article continues that research with an expanded dataset, examining empirically the relationship between research and development timelines, on the one hand, and effective patent life, on the other hand. It fills a conspicuous gap in our knowledge. Few scholars have considered patent term restoration from an empirical perspective, none has used a dataset of this size and scope, and none has addressed the questions this Article addresses.²⁶

²⁰ See *infra* section I.C. and note 84.

²¹ See *infra* section I.C.; Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585.

²² 35 U.S.C. § 156.

²³ See *infra* section I.A..

²⁴ See *infra* section I.A.

²⁵ One recent study found that firms under-invest in the development of cancer drugs that require long-term trials. Eric Budish et al., *Do Firms Underinvest in Long-Term Research? Evidence from Cancer Clinical Trials*, 105 AM. ECON. REV. 2044, 2047 (2015).

²⁶ The two significant empirical pieces to date differ from this Article in scope and focus. First, in 2018, Professors Beall, Darrow, and Kesselheim published an examination of patent term restoration for the 170 best-selling new drugs that experienced generic market entry between 2000 and 2012. Reed F. Beall et al., *Patent Term Restoration for Top-Selling Drugs in the United States*, 24 DRUG DISC. TODAY 20 (2018). The Beall dataset is smaller than the dataset for this Article, which includes *all* patent term restoration grants for drugs and

The dataset relates to 642 approved drugs (including biologics) for which a patent was restored. This comprises *every* grant of patent term restoration for a drug between enactment of the statute in September 1984 and April 1, 2018, when data collection ended. Four conclusions from the analysis stand out.

First, a longer clinical period is associated with a shorter final effective patent life (meaning after restoration), and a longer period between patent filing and start of clinical trials is associated with a shorter final effective patent life.²⁷ Although the magnitude of the impact is small, the results are strongly statistically significant, confirming the hypothesis that longer premarket research and development programs lead to shorter effective patent life, even with patent term restoration.

Second, application of the five-year cap on patent term restoration makes it less likely the final effective patent life will come close to the 14-year outer limit envisioned by Congress in 1984.²⁸ Again, the magnitude of the impact is small, but the results strongly statistically significant.

Third, there is generally no relationship between the therapeutic category in which a drug falls and the drug's final effective patent life.²⁹

Fourth, certain aspects of the drug patent itself play an important role in determining its final effective life.³⁰ In the 1990s Congress changed how patent terms are calculated.³¹ In 1984, a patent lasted for 17 years from its issuance date.³² Now a patent lasts for 20 years from its application date.³³ And if the patent relates to an earlier-filed patent, the ("child") patent term lasts for 20 years from the earlier ("parent") patent application date.³⁴ In

biologics between enactment of the statute in 1984 and April 1, 2018, and which includes additional variables discussed in section III. Sections III and IV, *infra*, discuss the findings in the Beall paper. Second, in 2014 Jaime Cárdenas-Navia presented an analysis of all patents extended by PTO between enactment in 1984 and December 31, 2013. Jaime F. Cardenas-Navia, *Thirty Years of Flawed Incentives: An Empirical and Economic Analysis of Hatch-Waxman Patent Term Restoration*, 29 BERKELEY TECH. L. J. 1301 (2014). This Article does not consider the Cardenas-Navia findings, because his dataset includes not only human drugs and biologics, but also medical devices, food additives, and animal drugs. Each is subject to a different premarket review paradigm (for instance, food additives do not go through effectiveness testing), and the formulas governing patent term restoration differ. Several other pieces in the legal, economic, or policy literature offer less comprehensive empirical examinations of patent term restoration; we discuss some below, where relevant.

²⁷ See *infra* section IV.A.

²⁸ See *infra* section IV.C.

²⁹ See *infra* section IV.B.

³⁰ See *infra* section IV.A.

³¹ The Uruguay Rounds Agreement Act (URAA), Pub. L. No. 103-465, 108 Stat. 4983 (1994).

³² 35 U.S.C. § 154 (1982).

³³ 35 U.S.C. § 154 (2012).

³⁴ *Id.*

1984 policymakers chose to permit restoration of child patents, because these patents issued and therefore (under the patent law at the time) expired later, and restoring them would lead to a longer effective patent life.³⁵ When Congress changed the patent term in 1994, it did not consider the impact on patent term restoration.³⁶ And in this dataset, when the 20-year rule applies, having “child” status *decreases* effective patent life — the opposite of what lawmakers intended in 1984.³⁷

Together these findings suggest a conclusion that could have significant policy implications. Longer premarket trials mean shorter effective patent life — but not by much. In 1984, policymakers chose to allow drug companies to select later-issued patents for patent term restoration. The ability to select a later-issued *child* patent for restoration may have therefore mitigated the distorting effect of the premarket regulatory regime. But Congress effectively undid the 1984 decision, ten years later, without reflection. The change has made it important for companies to pick later-issued *original* patents to achieve the same result as intended in 1984 — fourteen years of effective patent life. But these patents generally do not cover the drug’s active ingredient; they cover other aspects of the drug. Some scholars refer to non-active-ingredient drug patents as “secondary” patents — though they are simply patents, like any other — and a growing body of literature criticizes these patents.³⁸ But policymakers selected a 14-year target for effective patent life target in 1984, and the findings here suggest that later-issued and later-expiring original patents may now be essential to hitting that target. This Article takes no position on the optimal length of drug patents or the optimal period of exclusivity in the market for drugs, but the findings in this Article may have implications for scholars and policymakers who question the need for multiple patents covering the same product.

This Article proceeds as follows. Section I describes the tension between patent law and the medicine approval framework in the United States, as well

³⁵ See *infra* section IV.A.

³⁶ See *infra* section IV.A.

³⁷ See *infra* section IV.A.

³⁸ Amy Kapczynski et al., *Polymorphs and Prodrugs and Salts (Oh My!): An Empirical Analysis of “Secondary” Pharmaceutical Patents*, 7 PLOS ONE 1 (2012) (“These patents are generally termed secondary because they are assumed to come later in the sequence of innovation, and to offer less robust protection than a chemical compound claim. We use the term not because we believe these patents to be necessarily of lesser importance or strength, but because the term is conventional in the literature, and among practitioners.”); Cynthia M. Ho, *Should All Drugs Be Patentable? A Comparative Perspective*, 17 VAN. J. ENT. & TECH. L. 295 (2015) (criticizing practice of securing “secondary” patents and questioning their validity); Feldman, *supra* note 1 (examining and criticizing the practice of securing secondary patents, on the theory that it “refreshes” the monopoly protection on a drug).

as the patent term restoration framework enacted to partially mitigate this tension. Section II describes the hypotheses that motivated this project. Section III describes the dataset and findings. These comprise descriptive statistics relating to effective patent life (the time from FDA approval to patent expiry) and the impact of patent term restoration on effective patent life, as well as the results of a series of regressions assessing the determinants of effective patent life. Section IV discusses the findings, and section V concludes with thoughts about policy implications.

I. BACKGROUND

Firms considering the development of new medicines face both a distortion of their patents and a paradox.³⁹ Federal law stimulates scientific progress by ensuring that innovators can enjoy a period of exclusivity in their inventions, meaning a period during which others may not make or sell the inventions without their permission.⁴⁰ This period is made possible in part through the protection of patents, which last for a fixed period.⁴¹ But federal law also prohibits the sale of a new medicine until the inventor has performed years of testing in humans and persuaded the government that the medicine meets a particular regulatory standard of safety and effectiveness.⁴² This takes a variable amount of time — sometimes only a few years, but sometimes a decade or more.⁴³ This is patent distortion: mandatory testing wastes patent life, leaving inventors of regulated products less time (than other inventors) to commercialize their inventions without copies in the market. So long as the patent term starts before clinical testing ends, the longer clinical testing takes, the less patent life remains at the time of approval. This is the paradox: if a premarket testing program is more time-consuming, the U.S. legal system provides *less* of a reward to the inventor.

³⁹ See generally *see generally* Erika Lietzan, *The Drug Innovation Paradox*, 83 MO. L. REV. 39 (2018).

⁴⁰ See *infra* section I.B.

⁴¹ See *infra* section I.B.

⁴² See *infra* section I.A. The logistics are more complex in practice. The inventor is a natural person. That natural person *or* an entity to which the person has assigned the invention (for instance, the inventor's employer) may apply for the patent. 35 U.S.C. § 118. In the case of a new medicine, a company (such as the inventor's employer) generally performs or pays for this testing. This company is the medicine's developer. The distinction between the natural person and the company is immaterial for the point in the text: a medicine embodying the invention cannot be sold commercially until the testing is complete. This Article uses the term "inventor" to refer to the individual *and* the company authorized by the inventor.

⁴³ See *infra* section I.A.

A. New Drug and Biological Product Approval

By the time a new medicine reaches patients, it has been the subject of years — sometimes more than a decade — of testing, as well as intense review by FDA. Two federal statutes require premarket approval of new medicines: the Public Health Service Act (PHSA) requires that biological products (or “biologics”) be “licensed” before they are marketed, and the Federal Food, Drug, and Cosmetic Act (FDCA) requires that all other drugs be “approved” before they are marketed.⁴⁴ This Articles refers to both as “drugs” — which they are⁴⁵ — unless it is important to distinguish between biological and non-biological drugs, and it refers to the marketing authorization decision as “approval.”

New drug research and development usually begins with the discovery or creation of a molecule with useful biological activity — typically shown in tissues and in animal models.⁴⁶ This molecule eventually becomes the active moiety in a finished product for patients. FDA does not approve active moieties, however, nor does it approve based on useful biological activity. Instead, it approves a finished product — the active moiety in a formulation with inactive ingredients (such as buffers and excipients), with a particular route of administration, dosage form, and strength — for specific conditions of use (a particular disease or disease state, following a particular dosing regimen, with other relevant instructions for use).⁴⁷ It also approves labeling for prescribers that describes the approved conditions of use.⁴⁸ The precise medical condition for which the drug is approved is known as the drug’s “indication,” and the product must be shown safe and effective for that indication under the conditions of use described in its labeling.⁴⁹

Developing the evidence of safety and effectiveness needed for approval is a multistep process that begins with laboratory and animal testing and proceeds through several phases of clinical trials. Trials in humans typically start with small safety tests in healthy subjects and move through additional phases of progressively larger trials with more ambitious goals.⁵⁰ The process typically culminates in two randomized double-blinded controlled

⁴⁴ 21 U.S.C. § 355(a); 42 U.S.C. § 262(a).

⁴⁵ See 21 U.S.C. § 321(g) (defining drug).

⁴⁶ See Erland Stevens, MEDICINAL CHEMISTRY: THE MODERN DRUG DISCOVERY PROCESS 15, 95-100 (2014); Bruce H. Littman, *Translational Medicine: Definition, History, and Strategies*, in TRANSLATIONAL MEDICINE AND DRUG DISCOVERY 4-6 (Bruce H. Littman & Rajesh Krishna eds., 2011).

⁴⁷ 21 U.S.C. § 355(d); see also Lietzan, *Innovation Paradox*, *supra* note 39, at 55-56.

⁴⁸ 21 U.S.C. § 355(d).

⁴⁹ 21 U.S.C. § 355(d).

⁵⁰ 21 C.F.R. § 312.21; Institute of Medicine, TRANSFORMING CLINICAL RESEARCH IN THE UNITED STATES 24-26 (2010).

clinical trials.⁵¹ If these trials are large enough to permit meaningful conclusions, they can identify causal relationships — proving that the drug is effective.⁵² Empirical studies consistently find that for a new molecule this process can take 12 years or more.⁵³ The process is expensive and the outcome uncertain.⁵⁴

As a practical matter, the design and length of any particular premarket program depends on factors over which the developer has little control: the

⁵¹ The gold standard for FDA approval is an application containing positive results from two randomized, controlled, double-blinded, prospective interventional trials. Vinay Prasad & Vance Berger, *Hard-Wired Bias: How Even Double-Blind Randomized Controlled Trials Can Be Skewed from the Start*, 90 MAYO CLIN. PROC. 1171 (2015) (“Well-designed, adequately-powered randomized controlled trials ... are rightfully considered the highest form of evidence on which to base treatment and diagnostic decisions, minimizing potential biases, particularly confounding, that plague alternate, lesser forms of evidence.”). Double blinding means neither the patients nor the investigators know the assignments. Randomization and double-blinding reduce the potential for both bias and confounding (unaccounted-for variables that are actually responsible for the outcome). Thomas R. Frieden, *Evidence for Health Decision Making — Beyond Randomized Controlled Trials*, 377 N. ENG. J. MED. 465 (2017); see also 21 C.F.R. § 314.126 (describing the design characteristics of an adequate and well-controlled trial); FDA, GUIDANCE FOR INDUSTRY: CHOICE OF CONTROL GROUP AND RELATED ISSUES IN CLINICAL TRIALS (2001) (describing nature and purpose of randomization, controls, and double-blinding).

⁵² Frieden, *supra* note 51, at 470. Smaller trials usually have wider confidence intervals around effectiveness — meaning that the true value (actual effectiveness) could be anywhere within a larger range of numbers.

⁵³ Joseph DiMasi et al., *Trends in risks associated with new drug development: success rates for investigational drugs*, 87 CLIN PHARMACOL THER. 272 (2010) (noting that analyses across all therapeutic areas indicate that the development of a new medicine, from target identification through approval for marketing, takes over 12 years and often much longer).

⁵⁴ See Joseph A. DiMasi et al., *Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs*, 47 J. HEALTH ECON. 20 (2016) (estimating average out-of-pocket cost per approved compound of \$1.4 billion and total preapproval cost of \$2.56 billion); Erika Lietzan, *The Myths of Data Exclusivity*, 20 LEWIS & CLARK L. REV. 91, 107-08 (2016) (discussing range of estimates for the length of time and cost of developing a new drug); Chi Heem Wong et al., *Estimation of Clinical Trial Success Rates and Related Parameters*, 20 BIOSTATISTICS 273, 277 (2019) (examining over 21,000 compounds in trials between January 1, 2000, and October 31, 2015, and finding that only 13.8 percent of all drug development programs eventually lead to approval); Katarzyna Smietana et al., *Trends in Clinical Success Rates*, 15 NATURE REV. DRUG DISCOV. 379 (2016) (examining approvals in 2012-2014 and finding that small molecule drugs had only a 9 percent chance of making it from initial trials to commercial launch, and biological drugs an 18 percent chance); Helen Dowden & Jamie Munro, *Trends in Clinical Success Rates and Therapeutic Focus*, 18 NAT. REV. DRUG DISCOV. 495 (2019) (using data from 2015-2017 and finding the probability of launch from the start of clinical trials to be less than 10 percent); Government Accountability Office, NEW DRUG DEVELOPMENT: SCIENCE, BUSINESS, REGULATORY, AND INTELLECTUAL PROPERTY ISSUES CITED AS HAMPERING DRUG DEVELOPMENT EFFORTS 25 (Nov. 2006) (noting that clinical trial failure rates increased to 91 percent during the period 2000 through 2003).

type of molecule at issue, its mechanism of action, the disease itself and the biological pathways it uses, the specific disease state targeted, the therapeutic outcome tested, and even the presence and nature of other treatments on the market.⁵⁵ And the way these factors affect premarket timelines is also largely beyond the developer's control.⁵⁶ The developer has general choices — such as whether to proceed and (perhaps) which of several potential indications to pursue (or pursue first) — but much of the rest will be dictated by science, regulatory requirements, or FDA's policies and preferences.⁵⁷ Certain therapeutic categories are, however, consistently associated with longer premarket clinical programs. One recent article examining 570 new drug applications (for non-biologic drugs) approved between August 1984 and August 2016 found that antipsychotics, central nervous system agents, antidepressants, anticonvulsants, anti-Parkinson's agents, immunological agents, blood products, antiemetics, and antineoplastic agents were associated with longer clinical programs than non-biologic drugs in other therapeutic categories.⁵⁸

B. Patenting New Drugs and Biologics

The primary incentive to discover and develop a new drug in the United States is the prospect of a period for exclusive marketing — sales without competition from copycat products.⁵⁹ Several features of federal law make

⁵⁵ Lietzan, *Innovation Paradox*, *supra* note 39, at 62-77.

⁵⁶ *Id.* at 62.

⁵⁷ *Id.*

⁵⁸ *Id.* at 101-102. The drugs in these therapeutic categories had average clinical testing periods exceeding the overall average of the dataset (5.96 years). *Id.* at 88. See also Erika Lietzan & Kristina M.L. Aciri, *The Innovation Paradox: Pharmaceutical Marketing Exclusivity and Incentives for Drug Development*, 10 J. PHARM. HEALTH SERV. RES. 169 (2019) (discussing same results); Tufts Impact Report, *CNS Drugs Take Longer to Develop, Have Lower Success Rates, Than Other Drugs* (Nov/Dec. 2014) (finding that mean clinical development time for CNS drugs between 1999 and 2013 was 12.8 months, or 18%, longer than the mean time for other drugs); Joseph DiMasi et al., *R&D Costs and Returns by Therapeutic Category*, 38 DRUG INFO. J. 211, 217 (2004) (finding that the “mean overall time from initiation of clinical testing to marketing approval is 32% below average for analgesic/anesthetic drugs, 30% below average for anti-infective drugs, 9% below average for cardiovascular drugs, and 27% above average for [central nervous system] drugs”).

⁵⁹ See *supra* note 7; see also Kristina M.L. Aciri, *Economic Growth and Prosperity Stems from Effective Intellectual Property Rights*, 24 GEO. MASON L. REV. 865, 868 (2017) (“Without patent protection, and other forms of intellectual property rights to protect an innovator's investment, pharmaceutical drug development will not take place.”); *id.* n. 9 (listing scholars who have “demonstrated that patents foster *ex ante* innovation, motivating the investment of time and talent because of the prospect of financial gain from those endeavors”); Fabian Gaessler & Stefan Wagner, *Patents, Data Exclusivity, and the Development of New Drugs*, working paper, Searle Center, Northwestern University 4 (2018)

this period of exclusive sales possible, one of which is the protection of patents associated with the drug.

Federal law permits a patent to issue for any new and useful, non-obvious invention,⁶⁰ and a new drug *product* may encompass several patentable inventions. These usually include the product's active ingredient, which is the component intended to furnish the product's pharmacological activity or direct effects.⁶¹ The active ingredient patent is the most important patent for the inventor, because it usually aligns with the regulatory requirements governing approval of copies. That is, a competitor may file an "abbreviated" application for a generic copy of a non-biological drug, provided the application shows the generic drug's active ingredient is the same.⁶² An abbreviated application omits the safety and effectiveness data that the inventor was required to include, and it is correspondingly faster to prepare and much cheaper — perhaps a few million dollars, compared with the one or two billion spent by the inventor.⁶³ But the generic pathway is available only if the active ingredient is the same, so the active ingredient patent generally is key to ensuring a period without generic competition.⁶⁴ So too with biosimilar copies of biologics.⁶⁵ The applicant must show that its product is "highly similar" to the inventor's product,⁶⁶ which requires a comparative showing at the active ingredient level and usually implicates the

([here](#)) ("Our results indicate that a reduction in the overall duration of market exclusivity causally lowers the likelihood of project completion significantly. In fact, we find that the loss of one year of market exclusivity lowers the likelihood of drug approval by about 3.9%."); Aaron S. Kesselheim et al., *Determinants of Market Exclusivity for Prescription Drugs in the United States*, 177 JAMA INT. MED. 1658 (2017) ("In the pharmaceutical market, patents are considered essential to provide sufficient return on investment in drug development, which can take many years.").

⁶⁰ 35 U.S.C. § 101. Various other conditions must be satisfied for a patent to issue. *E.g.*, 35 U.S.C. § 112 (written description requirement).

⁶¹ 21 C.F.R. § 314.3.

⁶² 21 U.S.C. § 355(j)(2)(A) (authorizing submission of an abbreviated new drug application (ANDA)).

⁶³ CBO Cost Estimate (S.1695), Biologics Price Competition and Innovation Act of 2007, As Ordered Reported by the S. Comm. on Health, Education, Labor, and Pensions on June 27, 2007 ([here](#)) (noting that cost of developing a generic drug is \$1-\$5 million); *compare* note 54, *infra*.

⁶⁴ The drug statute also permits semi-abbreviated applications for drugs that have different active ingredients from their "reference" products, *see* 21 U.S.C. § 355(b)(2), but these are not generic copies, and they are beyond the scope of this Article.

⁶⁵ Although the drug statute requires a generic drug to have the "same" active ingredient as the innovative product on which it is based, the biologics statute permits a biosimilar biologic to be simply "highly similar" with "minor differences in clinically inactive components." *Compare* 21 U.S.C. § 355(j)(2) with 42 U.S.C. 262(i). This Article refers to both generic drugs and biosimilar biologics as "copies" for convenience.

⁶⁶ 42 U.S.C. § 262(i), (k).

active ingredient patent.⁶⁷

Conventional wisdom holds that firms developing drug products should file their active ingredient patents before they begin testing any formulation of the active ingredient in humans.⁶⁸ Various doctrines of patent law provide a strong incentive to file this application as early as possible.⁶⁹ Patent law also permits early filing; the law requires proof of “utility” which, for a drug, can ordinarily be shown with evidence from laboratory and animal testing.⁷⁰ Empirical research suggests that the earliest patent filing for new drugs occurs well before the first human trials.⁷¹

In the ordinary course of events, an inventor submits a patent application to the PTO for examination, and after the examination process — which may include communications between the applicant and examiner as well as amendments to the patent claims — the PTO will either issue or reject the

⁶⁷ E.g., FDA, GUIDANCE FOR INDUSTRY: SCIENTIFIC CONSIDERATIONS IN DEMONSTRATING BIOSIMILARITY TO A REFERENCE PRODUCT 9-10 (Apr. 2015).

⁶⁸ See, e.g., Roin, *Unpatentable Drugs*, *supra* note 7, at 539 (stating that “[p]harmaceutical patents are typically filed when drugs are in early preclinical research”); Rebecca S. Eisenberg, *The Role of the FDA in Innovation Policy*, 13 MICH. TELECOMM. & TECH. L. REV. 345, 348 (2007) (noting that applications for “composition of matter” patents are filed before clinical testing of a molecule begins).

⁶⁹ For example, a patent will generally be denied if the invention was in public use for more than a year before the patent application was filed. 35 U.S.C. § 102.

⁷⁰ U.S. Patent and Trademark Office, MANUAL OF PATENT EXAMINING PROCEDURE (MPEP) 2107.03 (9th ed. 2018) (requiring evidence “that reasonably supports” pharmacological or therapeutic utility and noting that data from in vitro or animal testing “is generally sufficient”); see *Nelson v. Bowler*, 626 F.2d 853, 856 (C.C.P.A. 1980) (finding utility based on data showing pharmacodynamic activity in animals, specifically, stimulating smooth muscle tissue in gerbils and modulating blood pressure in rats); *Cross v. Iizuka*, 753 F.2d 1040, 1052 (Fed. Cir. 1985) (finding utility on basis of in vitro demonstration of the claimed biological activity— preventing aggregation of platelets); see also *In re Brana*, 51 F.3d 1560, 1567 (Fed. Cir. 1995) (noting that “proof of an alleged pharmaceutical property for a compound by statistically significant tests with standard experimental animals is sufficient to establish utility” and stating court’s “firm conviction that one who has taught the public that a compound exhibits some desirable pharmaceutical property in a standard experimental animal has made a significant and useful contribution to the art, even though it may eventually appear that the compound is without value in the treatment in humans” (quoting *In re Krimmel*, 292 F.2d 948, 953 (C.C.P.A. 1961))).

⁷¹ Lietzan, *Innovation Paradox*, *supra* note 39, at 86 (examining 570 new drug applications approved between August 1984 and August 2016 and finding an average gap of 5.61 years between (1) the date of filing of the earliest-filed patent covering the drug or a method of using the drug and (2) the date FDA permitted clinical trials to begin); Michael K. Dunn, *Timing of Patent Filing and Market Exclusivity*, 10 NAT. REV. DRUG DISCOV. 487, 488 (2011) (examining the relationship between initial filing date of the earliest patent application and final effective patent life, which the author refers to as “market exclusivity,” and illustrating that the initial patent filing date is consistently before the start of clinical trials).

patent (in whole or in part).⁷² Sometimes however, the applicant will file *another* application relating to the same invention, citing the same subject matter or (depending on the application type) adding new subject matter. A “continuation” application cites the same subject matter, a “continuation-in-part” application may add subject matter.⁷³ In this Article, consistent with conventions in patent law, we refer to these two types of applications as *parent* (or *original*) applications and *child* applications — and the resulting patents as *parent* (or *original*) patents, and *child* patents. In other situations, the patent examiner may conclude that the application describes more than one invention and may require that the applicant select only one to prosecute; in this case, the applicant may place the other inventions in separate “divisional” applications.⁷⁴ We refer to these, also, as *child* applications and the resulting patents as *child* patents.

In addition to an active ingredient patent, a drug’s developer might hold a patent claiming the formulation or composition of the finished product, meaning the particular combination of active and inactive ingredients.⁷⁵ It might hold a patent claiming a particular dosage form and dosage of the active ingredient or formulation.⁷⁶ Other possibilities include a patent claiming a method of using or administering the product, a patent claiming the manufacturing process, and a patent claiming a metabolite of the active ingredient.⁷⁷ These patents may relate back to and reference the earlier application, and some could even be continuation or continuation-in-part patents. But it is also possible for a medicine’s developer to hold a new patent claiming another invention relating to the drug, which it sought during the premarket research program and which does not relate back to an earlier application.

C. Patent Term Distortion

⁷² 35 U.S.C. § 132.

⁷³ MPEP 201.07-201.09. Continuation and continuation-in-part applications can respond to new information that became available after the original filing. *Id.* For instance, a continuation application may make new claims, based on the disclosure in the original application. A continuation-in-part application may add subject matter *and* make new claims, which might be desirable if the inventor changed the invention after filing the original application.

⁷⁴ MPEP 201.06. Divisional applications are limited to the subject matter disclosed in the parent application. *Id.*

⁷⁵ 21 C.F.R. § 314.53(b). An inactive ingredient is any component other than the active ingredient, such as an excipient, preservative, solvent, buffer, or coating. 21 C.F.R. § 314.3.

⁷⁶ 21 C.F.R. § 314.53(b).

⁷⁷ 21 C.F.R. § 314.53(b); *see generally* John R. Thomas, PHARMACEUTICAL PATENT LAW 38-46 (2005) (listing various types of drug patent claims).

In 1962, Congress amended the FDCA to require that firms obtain preapproval of their new drugs and to require that their applications include proof of effectiveness (in addition to safety, which the statute had already required).⁷⁸ FDA's expectations about the content and scope of marketing applications grew more rigorous over the decades that followed.⁷⁹ The period from the first test in humans to the first commercial sale expanded, with predictable result: the amount of patent life remaining, by the time companies launched their drugs, grew shorter.⁸⁰ These remaining years are the "effective" life of the patent — the years during which the inventor may lawfully exploit the invention in the market, without others also selling the invention.

As noted, a drug inventor usually files the first patent application before starting clinical trials, which would generally lead to patent issuance at the beginning of (or during) clinical trials.⁸¹ During these decades, and indeed until the mid-1990s, a patent lasted for 17 years from issuance.⁸² As clinical programs grew longer, the effective life of this patent therefore grew shorter. If the patent applicant filed a continuation or continuation-in-part application, the patent might issue later in time and thus expire later, but so long as the patent issued during the premarket program, some portion of the term would be sacrificed.⁸³ Economic studies in the 1970s and early 1980s showed that drug effective patent life had plummeted since the 1962 amendments.⁸⁴ Concern about the diminishing effective patent life, combined with studies finding a decline in the rate of new drug introductions over the same years, led to proposals that lost patent life be restored to inventors after drug

⁷⁸ Drug Amendments of 1962, Pub. L. No. 87-781, § 103, 76 Stat. 780, 783 (1962).

⁷⁹ Lietzan, *Innovation Paradox*, *supra* note 39, at 52-54.

⁸⁰ Erika Lietzan, *The History and Political Economy of the Hatch-Waxman Amendments*, 49 SETON HALL L. REV. 53, 68 (2019).

⁸¹ See *supra* note 71; see also F.M. Scherer, *Pricing, Profits, and Technological Progress in the Pharmaceutical Sector*, 7 J. OF ECON. PERSPECT. 97, 100 (1993) (noting that "patents on new drug chemical entities were typically obtained at about the time when clinical testing began" when section 156 was enacted).

⁸² 35 U.S.C. § 154 (1984).

⁸³ Lietzan, *Political Economy*, *supra* note 80, at 65.

⁸⁴ E.g., David Schwartzman, *INNOVATION IN THE PHARMACEUTICAL INDUSTRY* 173 (1976) (finding that average effective patent life for new drugs had dropped to 13.9 years by the late 1960s and that it dropped to 12.4 years by the early 1970s); Martin M. Eisman & William M. Wardell, *The Decline in Effective Patent Life of New Drugs*, 24 RES. MGMT. 18, 20 (1981) (finding that average effective patent life dropped to 9.5 years by 1979); Peter Barton Hutt, *The Importance of Patent Term Restoration to Pharmaceutical Innovation*, 1 HEALTH AFFS. 6, 16-17 (1982) (discussing other studies); Leonard G. Schiffrin, *Lessons from the Drug Lag: A Retrospective Analysis of the 1962 Drug Regulations*, 5 HARV. J. L. & PUB. POL'Y (1982) (discussing other studies); see generally Lietzan, *Political Economy*, *supra* note 80, at 66-68.

approval.⁸⁵

D. Patent Term Restoration

In 1984, these proposals bore fruit with enactment of section 156 of the Patent Act, part of a broader piece of legislation that also created a statutory pathway for approval of generic drug applications.⁸⁶ The basic approach of section 156 has not changed since 1984. It permits extension of a patent claiming a drug, a method of using the drug, or a method of manufacturing the drug, if the drug was subject to a “regulatory review period” before commercial marketing or use.⁸⁷ Put more simply, restoration is available for a patent claiming a drug product that went through premarket approval.

The PTO will restore a patent subject to three conditions.⁸⁸ First, PTO must deny patent term restoration if FDA has already approved the active ingredient (or its salt or ester) pursuant to another application filed under the same FDA approval provision.⁸⁹ If the patent proposed for restoration claims

⁸⁵ Lietzan, *Political Economy*, *supra* note 80, at 70-71, 77.

⁸⁶ Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585.

⁸⁷ 35 U.S.C. § 156(a). For a drug, the “regulatory review period” is the period combining (1) the clinical testing period, which begins when FDA authorizes clinical trials by permitting an investigational new drug application (IND) to go into effect and which ends when the company submits its new drug application (NDA) or biologics license application (BLA), and (2) the approval period, which begins when the company submits its NDA or BLA to FDA and ends when FDA approves that application. 35 U.S.C. § 156(g).

⁸⁸ The statute also imposes procedural requirements. For instance, the patent owner must submit its request within 60 days of FDA approval. 35 U.S.C. § 156(d). As a result of a court ruling in 2010 and a legislative change in 2011, PTO counts every calendar day beginning on the first business day after FDA approval. *Medicines Co. v. Kappos*, 731 F.Supp.2d 470 (E.D. Va. 2010) (requiring Office to use a business day counting approach, meaning that the 60 days would begin on the first business day after FDA approval if that approved did not occur on a business day); *Leahy-Smith America Invents Act*, Pub. L. No. 112-29 (basically codifying this court decision); 35 U.S.C. § 156(d) (last two sentences). A statutory change in 2015 changed the deadline for controlled substances subject to scheduling decisions: the deadline is 60 days after FDA approval *or* issuance of an interim final rule scheduling the drug, whichever is later. *Improving Regulatory Transparency for New Medical Therapies Act*, Pub. L. No. 114-89; 35 U.S.C. § 156(i).

⁸⁹ The permission for commercial marketing after the regulatory review period must be the first permitted commercial marketing of the “product” under the provision of law under which the regulatory review period occurred. 35 U.S.C. § 156(a)(5)(A). The term “product” means the “active ingredient . . . including any salt or ester of the active ingredient.” 35 U.S.C. §§ 156(f)(1), (2). The statute does not define “active ingredient,” however, and PTO’s approach to the term has changed. In 2010 the Federal Circuit rejected PTO’s approach of considering whether FDA had previously approved any drug containing the same underlying active moiety, and PTO has since focused on whether FDA has approved a drug with the same active ingredient. *Photocure ASA v. Kappos*, 603 F.3d 1372 (Fed. Cir.

a method of manufacturing a product using recombinant DNA technology, however, the regulatory review period must represent the first commercial marketing of a product manufactured using the process.⁹⁰ Second, PTO may extend only one patent for each regulatory review period.⁹¹ In practice this means one patent for each approved marketing application. This does not, however, mean one patent for each new active ingredient. FDA sometimes requires companies to submit separate marketing applications at the same time for a single new active ingredient.⁹² If FDA approves these marketing applications on the same day, PTO will extend a patent for each application. Third, PTO may extend a patent only if it has not already extended the patent under section 156 (for instance in connection with a different drug).⁹³

PTO does not restore all days lost to premarket research and development. Patent life lost to animal and laboratory testing for FDA purposes is not recoverable, even if these studies involve far more than would be needed to secure a patent. Instead, PTO restores the days lost to clinical testing and FDA review of the marketing application, subject to five limitations which it applies in the order that follows. First, PTO does not restore any portion of the regulatory review period before patent issuance.⁹⁴ Second, PTO does not restore any portion of the regulatory review period during which the applicant did not act with due diligence.⁹⁵ Third, it restores only half of the testing period after patent issuance.⁹⁶ It restores every day of the approval period. Fourth, it restores no more than five years.⁹⁷ There is a different cap for a patent issued before enactment (September 24, 1984) if the product was already in clinical trials — but not approved — on that date. For these

2010). At FDA, the “active moiety” is the molecule responsible for the physiological or pharmacological action of the drug, while the active ingredient is the substance introduced to the body. 21 C.F.R. § 314.108(a); *Abbott Labs v. Young*, 920 F.2d 984, 988 (D.C. Cir. 1990).

⁹⁰ 35 U.S.C. § 156(a)(5)(B).

⁹¹ *Id.* § 156(c)(4).

⁹² For example, FDA requires separate marketing applications for different dosage forms and for different routes of administration. See FDA, GUIDANCE FOR INDUSTRY, SUBMITTING SEPARATE MARKETING APPLICATIONS AND CLINICAL DATA FOR PURPOSES OF ASSESSING USER FEES 3 (Dec. 2004) Also FDA sometimes splits marketing applications by indication, typically so that different review divisions can review the indications.

⁹³ 35 U.S.C. §§ 156(a)(2), (c)(4). Interim extensions, discussed in the text, do not count.

⁹⁴ 35 U.S.C. § 156(c).

⁹⁵ *Id.* § 156(c)(1). As of April 1, 2018, FDA had never adjusted its calculation of the regulatory review period after finding the patentee failed to act with due diligence. One applicant for patent term restoration admitted a lack of due diligence for 935 days, during which the IND was inactive. PTO subtracted these days from the testing phase. Corrected Notice of Final Determination, *In re: Patent Term Extension Application for U.S. Patent No. 5,681, 814* (Apr. 18, 2007).

⁹⁶ 35 U.S.C. § 156(c)(2).

⁹⁷ 35 U.S.C. § 156(g)(6).

“pipeline” drugs, PTO restores no more than two years.⁹⁸ Finally, the effective patent life after patent term restoration may not exceed 14 years.⁹⁹ Put another way, the expiry date of the restored patent must be no later than the 14-year anniversary of FDA’s approval of the marketing application.

In 1993, Congress amended the statute to permit interim grants of patent term restoration, which tide a patentee over until FDA approval of the marketing application and PTO’s decision on the patent term restoration request.¹⁰⁰ First, subsection (d)(5) authorizes one-year interim extensions if the FDA approval process would extend past patent expiry.¹⁰¹ PTO will not issue a (d)(5) extension, however, unless FDA has already accepted the marketing application.¹⁰² A (d)(5) interim extension ends 60 days after marketing approval, which coincides with the deadline to apply for ordinary (non-interim) patent term restoration.¹⁰³ Second, subsection (e)(2) authorizes one-year interim extensions after FDA approval, while PTO considers the request for restoration.¹⁰⁴ PTO will grant an (e)(2) extension without consulting FDA to determine whether the drug satisfies the eligibility standards.¹⁰⁵ With one exception, the total patent term extension including

⁹⁸ 35 U.S.C. § 156(g)(6)(C).

⁹⁹ 35 U.S.C. § 156(c)(3).

¹⁰⁰ Patent and Trademark Office Authorization Act of 1993, Pub. L. No. 103–179. This law took effect on December 3, 1993. Although subsection (e)(2) took effect in December 1993, PTO’s regulations already provided for one-year interim extensions when a complete PTR application had been submitted but PTO’s decision had not been issued. *See* 52 Fed. Reg. 9386, 9391 (Mar. 24, 1987) (explaining 7 C.F.R. § 1.760 (1987)).

¹⁰¹ 35 U.S.C. § 156(d)(5).

¹⁰² *E.g.*, Final Decision Regarding Interim Patent Extension Application Under 35 U.S.C. § 156(d)(5) for U.S. Patent No. RE41209 (Feb. 4, 2016). PTO reasons that the statute requires this, by stating that the applicant for patent term restoration must reasonably expect that the approval process “that began” for the product will extend past patent expiry. *Id.*

¹⁰³ 35 U.S.C. § 156(d)(5)(E).

¹⁰⁴ 35 U.S.C. § 156(e)(2).

¹⁰⁵ In one case, after granting two interim extensions, PTO denied restoration on eligibility grounds and rescinded the second interim extension. Initially, Johnson & Johnson (J&J) received two (e)(2) interim extensions for Vusion (miconazole nitrate, white petrolatum, and zinc oxide). The company had put forward a plausible argument that it was entitled to patent term restoration: zinc oxide had reached the market under an earlier version of section 505 of the FDCA that did not require premarket approval and did not involve proving effectiveness. *See* Response to Order to Show Cause, *In re. Patent of Charles E. Clum et al.*, Patent No. 4,911,932 (Sept. 8, 2008). But more than 20 years earlier, PTO had rejected identical reasoning in a matter involving a different drug—concluding that marketing ammonium lactate under an NDA submitted under this earlier version of section 505 constituted relevant commercial marketing under section 156. And in the earlier matter, a federal court had rejected the patent owner’s court challenge, deferring to PTO. *Westwood Pharmaceuticals, Inc. v. Quigg*, 1989 WL 205631 *3 (D.D.C. 1989). In the end, despite initially granting J&J two interim extensions, PTO concluded that the earlier precedent controlled. Denial of Patent Term Extension Application for U.S. Patent No. 4,911,932

interim extensions cannot exceed the extension for which the patentee would be eligible under section 156.¹⁰⁶ The exception is this: a pipeline drug is entitled to two years of effective patent life from the date of marketing approval regardless of any interims received.¹⁰⁷

II. HYPOTHESES

The discussion in the preceding subsections leads to several hypotheses. Without patent term restoration, longer premarket research and development programs should distort drug patents — lead to shorter effective patent life. And certain therapeutic categories should be associated with shorter effective patent life. Further, because the Patent Act does not restore every day of patent life lost to premarket research and development, this distortion should still be evident *after* PTO extends the patent term. Restoring only 50 percent of the days spent in clinical trials should preserve the distortion, because the patent owner will continue to lose days of patent life in proportion to the length of its clinical program. The five-year cap should have a more dramatic impact: once a clinical program reaches a certain length, more testing should simply translate to lost patent life — just as was the case before Congress enacted section 156. Hitting the five-year cap should mean a drug's final effective patent life will be shorter and less likely to reach 14 years.

Drugs with longer clinical programs, and drugs with longer overall premarket research and development programs, should be associated with application of the five-year cap. These drugs should be less likely to reach the 14-year maximum effective patent life, and they should be associated with a shorter final effective patent life. And some therapeutic categories — those associated with longer average clinical programs — should be associated with application of the five-year cap. These drugs should be less likely to reach the 14-year limit, and they should be associated with a shorter final effective patent life.

The 1994 change in the patent law leads to another hypothesis, but explaining the hypothesis requires a more detailed explanation of how the change was implemented. As already noted, in 1984 a patent lasted for 17 years from issuance.¹⁰⁸ In the Uruguay Rounds Agreement Act (URAA), Congress revised section 154 of the Patent Act, which governs the patent

(Mar. 19, 2009). Thus it concluded that Vusion did not represent the first permitted commercial marketing of miconazole nitrate or zinc oxide and that the patent did not claim white petrolatum, vacated the second interim extension, and denied patent term restoration.

¹⁰⁶ 37 C.F.R. §§ 1.760, 1.790(a).

¹⁰⁷ 35 U.S.C. § 156(d)(5)(E)(ii).

¹⁰⁸ 35 U.S.C. § 154 (1984).

term.¹⁰⁹ For patents issued on applications filed on or after June 8, 1995, the term is 20 years from the patent application or, if the application refers to an earlier-filed application, 20 years from the date of that application.¹¹⁰ Put another way, a child application expires 20 years after its parent application was filed. Complicating things further, patents in force on June 8, 1995, or that issued on applications filed before that date, received the benefit of this change in the law.¹¹¹ In other words, these “transitional” patents lasted either 20 years from application or 17 years from issuance, whichever ended later. The new calculation was more favorable if the PTO had issued the patent in fewer than 36 months *and* there were no earlier-filed applications. In these cases, the new calculation led to a revision of the expiration date in what came to be known as the “URAA extension.”

The relationship between the URAA extension and patent term restoration was briefly muddled. On June 7, 1995, PTO announced that patentees would enjoy either the URAA extension or patent term restoration — whichever was longer — but not both.¹¹² On October 16 of the same year, however, the Eastern District of Virginia ruled that a patentee was entitled to both.¹¹³ And then on April 4, 1996, the Federal Circuit took a different position.¹¹⁴ The owners of patents in force on June 8, 1995, were entitled to add patent term restoration to a 20-year patent term, *even if* PTO had already calculated restoration and issued a certificate.¹¹⁵ If, however, the patent was in force on June 8, 1995, *only* because of patent term restoration — i.e., it was then enjoying its restored days — the URAA extension was unavailable.¹¹⁶ PTO had been restoring patents all the while, and eventually restorations had to be recalculated to conform to the Federal Circuit ruling.

Drugs approved in the 35 years since enactment of section 156 have been protected by patents subject to three different patent term regimes: the pre-URAA regime of lasting for 17 years from issuance, the post-URAA regime of lasting for 20 years from application or parent application, and the transition regime.¹¹⁷ And most drugs were protected by more than one

¹⁰⁹ The Uruguay Round Agreements Act (URAA), Pub. L. No. 103–465, 108 Stat. 4983 (1994).

¹¹⁰ 35 U.S.C. § 154(a)(2).

¹¹¹ 35 U.S.C. § 154(c)(1).

¹¹² 60 Fed. Reg. 30309 (June 8, 1995).

¹¹³ *Merck & Co. v. Kessler*, 903 F.Supp. 964 (E.D. Va. 1995), *aff’d in part, rev’d in part*, *Merck v. Kessler*, 80 F.3d 1543 (Fed. Cir. 1996).

¹¹⁴ *Merck v. Kessler*, 80 F.3d 1543 (Fed. Cir. 1996).

¹¹⁵ 35 U.S.C. § 154(c)(1).

¹¹⁶ *Merck v. Kessler*, 80 F.3d at 1550.

¹¹⁷ This oversimplifies. In 1994 and again in 1999, Congress also enacted patent term adjustment to provide relief for the shortening of effective patent life stemming from delays at PTO. First, as part of the URAA, Congress provided for adjustment of the patent term to

patent.¹¹⁸ For any particular drug, these patents may have varied in scope (for example, active ingredient versus formulation) as well as type (child versus parent) and term (17 years from issuance versus 20 years from application). And the drug company could select any one of these patents for restoration. Because PTO will restore only a portion of the clinical trial period after patent issuance, selecting a child patent subject to a 17-year term should be associated with longer final effective patent life but restoring a child patent subject to a 20-year term should be associated with shorter final effective patent life, as follows.

Restoring a child patent should be associated with longer final effective patent life if that patent is subject to the 17-year patent term. Under this regime, if a company filed its application later, the resulting patent would generally issue later and therefore have a later expiry date. Because PTO will restore only the portion of the clinical trial period after patent issuance, less of the clinical period would be eligible for restoration. But the smaller number of restoration days would be added to a later expiry date. Because PTO restores only 50 percent of the time spent in trials, a restored later-issuing child 17-year patent would expire later than a restored earlier-issuing parent 17-year patent.

Conversely, restoring a child patent should be associated with a shorter final effective patent life if that patent is subject to the 20-year patent term. Under this regime, if a company files its application later, the resulting patent will generally issue later — but it will not have a later expiry date. The expiry date is now keyed to the date of the parent application. As before, PTO will restore only the portion of the clinical period after patent issuance, so less of the clinical period is eligible for restoration. But in this case, PTO will not be adding this smaller number to a later expiry date. This leads to the final hypothesis: restoring a child patent should be associated with longer effective patent life if the 17-year patent term applies, but not if the 20-year term applies.

compensate for delay because of an interference proceeding, secrecy order, or appellate review of an adverse decision on patentability. 35 U.S.C. § 154(b) (1995). This adjustment applied to patent applications filed on or after June 8, 1995, and before May 29, 2000. 21 C.F.R. § 1.701(e). Second, in 1999, Congress provided for automatic adjustment of the patent term to compensate for more routine delays at PTO. American Inventors Protection Act of 1999, Title IV of Pub. L. No. 106-113, at § 4402. Section 154(b) now states various deadlines for stages in the patent prosecution — such as three years for completion of the entire process (subject to various exceptions) — and generally requires a day of adjustment for each day of delay beyond the stated deadlines. 35 U.S.C. § 154(b). This scheme applies to patent applications filed after May 29, 2000. Pub. L. No. 106-113, at § 4405(a).

¹¹⁸ Patents issued after approval would not be among them (unless they were issued immediately after approval). A company must request patent term restoration within 60 days of receiving FDA approval. 35 U.S.C. § 156(d). *See supra* note 88.

Section III explores these questions examining all drug (including biologic) patent term restoration grants from enactment of the Hatch-Waxman Amendments on September 24, 1984, through April 1, 2018.

III. FINDINGS

A. Dataset and Methodology

The dataset used in this Article relates to 642 approved marketing applications for which a patent was restored. The dataset was generated as follows.

First, PTO provided a spreadsheet of all patent term restoration applications received between September 28, 1984, and April 1, 2017. PTO also maintains a table of patent term restoration grants on its website.¹¹⁹ Neither list is complete, so the lists were combined, and duplicates removed.¹²⁰ Second, drugs and biologics were extracted for analysis. Section 156 authorizes patent term restoration for other regulated products: food additives, color additives, animal drugs, and veterinary biologics. These were excluded.¹²¹

Third, we extracted the drugs and biologics for which PTO *granted* patent term restoration before April 1, 2018.¹²² In a handful of instances, FDA

¹¹⁹ PTO, *Patent Terms Extended Under 35 U.S.C. § 156* ([here](#)).

¹²⁰ For instance, the spreadsheet omitted — but the table included — Atrovent (ipratropium bromide). The table omitted — but the spreadsheet included — more than fifty new drugs with restored patents, including Savella (milnacipran hydrochloride), Potiga (ezogabine), and Myfortic (mycophenolic acid). Although some PTR applications could have been omitted from both sources, the Federal Register was used to confirm that PTO restored no other drug or biologic patent in the interval studied. PTO cannot restore a patent until FDA has published the regulatory review period in the Federal Register.

¹²¹ PTO's spreadsheet classified the products, but some products were misclassified. For instance, PTO lists Lac-Hydrin (ammonium lactate) and Nix (permethrin) as medical devices, although FDA approved them under new drug applications. PTO lists Luveris (lutropin alfa), Lantus (insulin glargine recombinant), Novolog (insulin aspart recombinant), Increlex (mecasermin recombinant), Iplex (mecasermin rinfabate recombinant), and Omontys (peginesatide acetate) as biologics, but FDA approved them under new drug applications. We categorized the products in the spreadsheet manually based on the regulatory review provisions — new drug approval, biologics license approval, medical device approval or clearance, new animal drug approval, or food additive petition — that were or would have been applied by FDA.

¹²² In most cases, we examined PTO's notice of final determination and the patent extension certificate, found in the Image File Wrapper available through PTO's Public Patent Application Information Retrieval (PAIR) system. PAIR was missing the relevant documents for some patents. In these cases, we relied on other sources of information. For instance, the PTO list of patent terms extended includes links to some certificates. Some notices of final determination are available through Westlaw, and others can be found

approved more than one marketing application for the same active ingredient on the same day, which allowed PTO to extend more than one patent.¹²³ In these situations, the lower-numbered (and thus earlier-filed) marketing application was extracted for analysis; the higher-numbered application was omitted. If a patent owner enjoyed interim extensions that ultimately equaled the number of days sought, we treated the restoration as granted — even if the PTO never ruled on the restoration request.¹²⁴ If the company ultimately received zero days of extension — because the effective patent life already exceeded fourteen years — we treated the restoration as denied.¹²⁵

Finally, we excluded drugs for which no investigational new drug application (IND) ever took effect. Federal law requires an IND for clinical trials if the drug in question will be shipped in interstate commerce.¹²⁶ The lack of an IND means the company performed its clinical trials overseas. These drugs were omitted from the dataset because the clinical trial period for purposes of patent term restoration begins on the IND effective date and was, therefore, zero days for these products — not a factually correct representation of the number of days spent in clinical testing.

The final dataset contains 642 drugs (also called “observations” in the statistical portion of this Article), for which we gathered other information as follows. First, we collected regulatory information about each drug: (1) the date on which the IND took effect, allowing the company to start clinical

through hyperlinks in a PTO list of notices mailed after November 1, 1996, and January 1, 2005 ([here](#)).

¹²³ See *supra* section I.D. Drug companies do not always seize the opportunity to restore more than one patent. For instance, twice Fujisawa asked for restoration of only one patent, even though FDA had approved two applications for the same active ingredient on the same day. The drugs in question were Prograf (tacrolimus) and Mycamine (micafungin sodium). PTO had even told the company that “two patents are eligible for extension based on the regulatory review periods for Mycamine (micafungin sodium) in NDA 21-506 and 21-754.” Notice of Final Determination and Requirement for Election, *In re Patent Term Extension Application for U.S. Patent No. 5,376,634* (Dec. 10, 2007). But Fujisawa declined to take this path. See Response to Requirement for Election Under 37 C.F.R. § 1.785 (“Applicants respectfully elect the Application for Patent Term Extension for U.S. Patent No. 6,107,458 based on NDA 21-506. Accordingly, Applicants respectfully withdraw the Application for Patent Term Extension of U.S. Patent No. 6,265,536 based on NDA 21-754.”).

¹²⁴ In nine instances, the patentee received all patent term restoration it had sought, through sequential interim extensions. We dropped four because FDA never calculated the regulatory review period (so we could not confirm the dates asserted by the applicant in its PTR application). We treated the remaining five as grants of PTR.

¹²⁵ This includes instances in which PTO initially granted an extension, but the URAA extension applied later and took the unrestored patent life past the 14-year limit, so no restoration was ultimately applied. This was true in the case of Zofran (ondansetron) and Suprane (desflurane), for instance.

¹²⁶ 21 U.S.C. §§ 355(a), (i).

trials, (2) the date on which the company submitted its marketing application, (3) the date on which FDA approved the application, (4) the length of the clinical testing period, and (5) the length of the FDA review period.¹²⁷ We also assigned each drug a therapeutic category.¹²⁸

Second, we collected information about each restored patent: (1) the date on which the inventor filed the patent application that led to issuance of the patent, (2) the date that would control calculation of a 20-year patent term under current law,¹²⁹ and (3) the date on which the patent issued, or the date on which the original patent issued in the case of a reissued patent.¹³⁰ The collected patent information also included (1) the type of term the patent enjoyed (17-year, 20-year, or transitional – and if so which),¹³¹ (2) whether the patent was a child patent, (3) the number of days of patent term adjustment, if any,¹³² (4) the original patent expiry date (after patent term adjustment) without patent term restoration,¹³³ (5) how PTO

¹²⁷ FDA publishes this information in the Federal Register when it calculates the regulatory review period.

¹²⁸ The methodology was crude. Some drugs in the dataset were withdrawn from the market years ago, and some were never launched in the United States. As a result, no readily available dataset provides a therapeutic category for every drug in the dataset. An orthogonal approach was adopted. For each drug, five factors were considered: the established pharmacological class assigned by FDA; the initial use for which the drug was approved; the category and class assigned in the U.S. Pharmacopoeia (USP) Medicare Model Guidelines for CMS Version 7.0; the anatomical therapeutic classification (ATC) assigned by the World Health Organization (WHO); and the category assigned by the National Institutes of Health (NIH) in its National Library of Medicine Drug Portal. Based on this information, each drug was placed in a category corresponding roughly to one of the categories in the USP guidelines.

¹²⁹ If the patent resulted from an original patent application with no reference to an earlier-filed U.S. application, the relevant date was the filing date of the application or, if applicable, the Patent Cooperation Treaty (PCT) filing date. If the patent resulted from an application that was a continuation, continuation-in-part, or division of an earlier-filed application, the new application necessarily cited the earlier application (and any earlier applications, in turn). In these cases, the relevant date was the earliest filing date of any related U.S. application referenced in the application. If the restored patent was a reissue of an earlier patent, our analysis identified the relevant date for the originally issued patent.

¹³⁰ A patent may be reissued to correct certain types of error; in this case the patent number changes (and now begins with “RE”) but the term remains the same. 35 U.S.C. § 251.

¹³¹ See *supra* section II.

¹³² See *supra* note 117. Patent term adjustment was generally taken from documents available on PAIR.

¹³³ Various sources report this information: the spreadsheet provided by PTO; the table of terms restored on PTO’s website; patent term restoration applications themselves; PTO’s notices of final determination; and for composition of matter and method of use patents covering new drugs, editions of the ORANGE BOOK published before patent expiry. (In this annual publication, FDA publishes the numbers and expiration date of every unexpired patent that claims an approved drug or method of using that drug. See FDA, APPROVED DRUG

calculated patent term restoration,¹³⁴ (6) whether PTO applied the five-year (or two-year) cap and 14-year limit,¹³⁵ (7) the number of days restored,¹³⁶ and (8) the final patent expiry date after restoration.¹³⁷ These entries reflect case-by-case judgment calls, based on the law and based on review and consideration of several sources for each patent. The goal in each case was to ensure that the patent term type, original expiration date, restoration award, and revised expiration date were internally consistent (each with the others), legally correct (considering changes in the law that applied during the patent life), and corroborated by at least one source.

Third, we gathered information about the lifecycle of the 554 non-biological drugs — but not the 88 biologics — in the dataset.¹³⁸ This included the number and filing date of every patent claiming the drug or an approved

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These sources sometimes contained errors, and in some cases the information reported was superseded by later events. For example, the spreadsheet from PTO contained typographical mistakes. In addition, some dates were later changed by patent term adjustment, *see supra* note 117, or the URAA extension, *see supra* section II. That is, PTO might have issued a final decision on patent term restoration before June 1995, relying on a 17-year term for the patent, and the term could have later shifted to a 20-year term. In this case PTO's notice of final determination would have calculated the restoration due and offered a revised expiration date based on adding those days to the original expiration date. When the patent later converted to a 20-year term, some of this information became incorrect, but PTO did not issue new documents. The dataset reflects the ultimate final expiry date after all adjustments were made.

It does not, however, capture terminal disclaimers filed later in the life of the patent. A terminal disclaimer causes the patent to expire on the same date as an earlier patent and is typically filed to avoid invalidation of the patent on "obviousness" grounds.

¹³⁴ This appears in the notice of final determination, and most notices are available on PAIR or (in a few cases) on Westlaw. Some contain mathematical or calendar errors, but in these cases the patent extension certificate is typically still correct.

¹³⁵ This appears in the notice of final determination. We corroborated it with the patent term extension certificate or the list of patent terms extended on PTO's website, or the ORANGE BOOK if neither of these sources provided the information needed. We confirmed application of the 14-year limit by comparing all final expiration dates with all FDA approval dates, and we confirmed application of the 2-year and 5-year caps by comparing final expiration dates with original expiration dates.

¹³⁶ We took this from the notice of final determination, if it was available on PAIR, the extension certificate, or the list of patent terms extended on PTO's website.

¹³⁷ We took this from the notice of final determination and corroborated it with at least one other source — typically the list on PTO's website, but in some cases the ORANGE BOOK. As explained in note 133, the dates reported in these documents were sometimes superseded by later events. In these cases the dataset reflects the corrected information, which was corroborated with at least one additional source whenever possible.

¹³⁸ The Hatch-Waxman Amendments included statutory authority to approve generic drugs, and FDA approved generic drugs throughout the period covered by our dataset. Congress did not enact comparable authority for biologics until 2010. Biologics Price Competition and Innovation Act of 2009, Pub. L. 111-148, 124 Stat. 119 (2010).

method of using the drug listed in the ORANGE BOOK before April 1, 2018.¹³⁹ This information is incomplete for antibiotics approved before 1997, because this publication omits patents on these drugs that expired before October 8, 2008.¹⁴⁰ The dataset also includes the date on which the company launched the non-biological drug in the market and the launch date of the first generic drug containing the same active ingredient.¹⁴¹

B. The Effect of Patent Term Restoration

The resulting dataset of drugs and biologics approved over more than 30 years provides a basis for robust description of average clinical trial program length, effective patent life before patent term restoration, and the impact of patent term restoration. The average clinical development program in the dataset is 6.04 years (median 5.29 years). This is consistent with the findings

¹³⁹ The patent numbers and expiration dates appear in the ORANGE BOOK. *See supra* note 133. The filing date for purposes of the dataset was the earliest filing date appearing on the face of the patent, considering patent filings in other countries and any provisional application filed in the United States.

¹⁴⁰ Before November 1, 1997, antibiotic drugs reached the market under section 507 of the FDCA rather than section 505 of the FDCA before November 1, 1997. 21 U.S.C. § 357 (1993) (repealed 1997). The Hatch-Waxman scheme did not apply to them, so they were not subject to patent listing requirements. The pre-1997 (“old”) antibiotics were not subject to listing requirements until October 7, 2008. Q1 Program Supplemental Funding Act of 2008, Pub L. No. 110–379, § 4(b), 122 Stat. 4075 (2008) (to be codified at 21 U.S.C. § 355); FDA, DRAFT GUIDANCE FOR INDUSTRY ON THE SUBMISSION OF PATENT INFORMATION FOR CERTAIN OLD ANTIBIOTICS, 73 Fed. Reg. 73,659 (Dec. 3, 2008). Beginning on October 8, 2008, the holders of approved applications for old antibiotics listed patents, including patents that had already issued, but they did not list expired patents. Thus, if a patent for an old antibiotic expired before that date, it would have never appeared in the ORANGE BOOK.

¹⁴¹ IQVIA provided the launch dates. We do not have complete launch date information, however, for four reasons. First, IQVIA reports only the month and year the drug is launched in the United States, so (for instance) it fails to distinguish between January 1 and January 31, which could be material for some analysis we perform. Second, we requested (and IQVIA provided) launch information only for drugs for which a patent had been restored by the spring 2017. Third, for some of these drugs, IQVIA lacked the data in question. Fourth, in several cases the launch date was not useable in our analysis. Launch dates before approval were treated as error. Launch dates more than six months after product approval were flagged for follow-up. In a handful of cases follow-up in other sources — typically trade press or securities filings — revealed a reason not to rely on the IQVIA date for purposes of the planned analysis. To give an example, Cesamet (nabilone) was launched, but then acquired by a second company and relaunched, and IQVIA reported only the relaunch date. In this case the IQVIA date was excluded. For quality assurance, the generic drug launch dates were also compared with information from FDA’s website about the timing of first generic approval, and other sources (such as trade press and securities filings) were used to investigate discrepancies. In a handful of cases, investigation led to exclusion of the IQVIA information.

of an earlier paper in this series, based on a smaller dataset that excluded biologics and ended one year earlier; the earlier study found an average of 5.96 years (median 5.23 years).¹⁴² The finding is also consistent with the findings of other scholars.¹⁴³

In this dataset, average effective patent life without restoration — meaning the time from FDA approval to the original expiration date of the patent — is 8.71 years (median 9.49 years). This is somewhat shorter than the average effective patent life reported in empirical studies that supported patent term restoration in the first place.¹⁴⁴ Whether effective patent life (before restoration) has changed over time is more complex. The average effective patent life of patents in the dataset has increased over the passage of time, in the sense that patents in the dataset issued in the later years of the interval studied have more life remaining after FDA approval than patents issued in the earlier years of the interval studied. As Figure 1 in the Appendix shows, patents in the dataset issued in the 1980s tended to have eight to ten years of life remaining after FDA approval, and patents issued in the 2000s have tended to have ten to twelve years of life remaining. But the average effective patent life for the *drugs* in the dataset has *not* increased over time: drugs approved in recent years tend to have around the same average effective patent life as drugs approved at the beginning of the interval studied. As Figure 2 shows, drugs approved in the 1980s tended to average eight to ten years of effective patent life, as did drugs approved in the 1990s, as have drugs approved in the 2000s.

The average amount of patent life restored in this dataset was 1049 days or 2.87 years (median 944 days, or 2.59 years). Others have reported similar numbers.¹⁴⁵ This does not represent the average that one would expect under

¹⁴² Lietzan, *Innovation Paradox*, *supra* note 39, at 88.

¹⁴³ E.g., Steven M. Paul et al., *How to improve R&D productivity: the pharmaceutical industry's grand challenge*, 9 NAT REV DRUG DISCOV. 903 (2010) (noting that the three clinical development phases take 1.5, 2.5 and 2.5 years, respectively, and the phase from submission to launch requires another 18 months); Kenneth Kaitin et al., *Pharmaceutical innovation in the 21st century: new drug approvals in the first decade, 2000–2009*, 89 CLIN PHARMACOL THER. 183 (2010) (noting that the average clinical development time for drugs approved between 2005 and 2009 was 6.4 years).

¹⁴⁴ See Schwartzman, *supra* note 84, at 173 (reporting that average effective patent life for new drugs had dropped to 12.4 years by the early 1970s); Eisman & Wardell, *supra* note 84, at 20 (finding that the average had dropped to 9.5 years by 1979).

¹⁴⁵ For instance, Professors Beall, Darrow, and Kesselheim reported a median restoration of 2.75 years in the 83 drugs of their dataset that received patent term restoration. Beall, *supra* note 26, at 20. In 1996, Professors Grabowski and Vernon found that the average patent term extension for new drugs coming to the market in the 1991 to 1993 period was 2.3 years. Henry Grabowski & John Vernon, *Longer Patents for Increased Generic Competition in the U.S.: The Hatch Waxman Act After One Decade*, 10 PHARMACOECONOMICS 110, 119–120, 121 (1996). And in 1998, the Congressional Budget

current law, because 113 drugs in the dataset were subject to the two-year cap.¹⁴⁶ With these drugs omitted, the average restoration for the remaining 529 drugs is 1117 days or 3.06 years.¹⁴⁷ The average effective patent life in the dataset after patent term restoration is 11.58 years (median 12.83 years).¹⁴⁸ This average is consistent with earlier reports examining drugs approved in the 1990s but lower than a figure reported for recently approved top-selling drugs.¹⁴⁹ Figure 3 in the Appendix shows that average effective patent life after restoration has not meaningfully changed since the late 1980s and that it varies less than effective patent life before restoration.

C. The Determinants of Effective Patent Life

We hypothesized that longer premarket research and development programs would lead to shorter effective patent life. We also hypothesized that because the statute does not restore every day of patent life lost to premarket testing, this effect would still be evident today. To assess these questions, we performed a series of regressions to identify the determinants of effective patent life both before and after PTO applies patent term restoration.¹⁵⁰

Office reported that the 51 new drugs approved between 1992 and 1995 that enjoyed patent term restoration received an average of 2.9 years. Congressional Budget Office, *HOW INCREASED COMPETITION FROM GENERIC DRUGS HAS AFFECTED PRICES AND RETURNS IN THE PHARMACEUTICAL INDUSTRY* 40 (July 1998). In 2008, however, Charles Clift reported that 26 of the top 40 best-selling drugs in 2006 benefitted from patent term restoration and received an average of 3.6 years. Charles Clift, *The Value of Patent Term Extensions to the Pharmaceutical Industry in the USA*, 5 J. GEN. MED. 201, 205-06 (2008).

¹⁴⁶ This includes two pipeline drugs with patents that expired before FDA approval, which therefore received two years of effective patent life from the date of FDA approval. See *supra* section I.D. These were Corlopan (fenoldopam mesylate) and Remeron (mirtazapine).

¹⁴⁷ In a counterfactual world in which only the five-year cap applied, the average restoration for the entire dataset of 642 drugs would have been 1186 days or 3.25 years.

¹⁴⁸ As discussed in section IV.C., however, if the two-year cap had not applied to 18 percent of the dataset, meaning in a counterfactual world in which only the five-year cap applied, the average would have been higher.

¹⁴⁹ Beall et al., *supra* note 26, at 21 (examining the 170 best-selling new drugs that experienced generic market entry between 2000 and 2012 and reporting a median effective patent life of 13.25 years for the 83 that received patent term restoration); but see Grabowski and Vernon, *supra* note 145, at 120 (reporting that new chemical entities approved from 1991 to 1993 had an average effective patent life, after restoration, of 11.8 years, which the authors claimed in 1996 was “probably representative of the average patent lives” of new chemical entities then coming onto the market); Congressional Budget Office, *supra* note 145, at 40 (reporting 11.6 years for the 51 new drugs approved between 1992 and 1995 that enjoyed patent term restoration).

¹⁵⁰ A regression analysis is a statistical process for mathematically establishing the relationships between variables and estimating their impact. In regression analysis, the

1. Effective Patent Life Before Patent Term Restoration

Using our full dataset of 642 observations, we performed regression analysis to assess which variables explain effective patent life before the award of patent term restoration (Regression 1).¹⁵¹ This regression had high explanatory power; in statistical terms, the adjusted R^2 was 0.84. In simple English, this means that 84 percent of the variation in the dependent variable (effective patent life) was explained by the independent variables found to have explanatory power. The results for Regression 1 appear in Table 1 in the Appendix and are summarized here.

Certain variables had negative coefficients, meaning that as they increase the effective patent life decreases. To begin with, the length of time between the patent (or if applicable, parent patent) filing date and the start of clinical trials was negatively correlated with effective patent life. We treat this period as a rough proxy for the preclinical testing period.¹⁵² The length of the clinical testing period was also negatively correlated with effective patent life. In statistical terms, the coefficients were small but strongly statistically significant — which means that the impact was small but unlikely to be a matter of chance.¹⁵³ We expected these results. We also investigated the possibility that certain therapeutic categories were negatively correlated with effective patent life before restoration and found that only one category (antipsychotics) had explanatory power. We did not expect this result. We discuss these findings in section IV.

We also assessed several independent variables relating to the type of

dependent variable is the main factor that one is trying to understand or predict, and the independent variables are factors believed to have an impact on the dependent variable. Several approaches can be used. The Appendix describes the regression models used.

¹⁵¹ This was a least squares regression analysis. Details can be found in the Appendix.

¹⁵² For this calculation, the filing date is the date that controlled (or would have controlled) calculation of the 20-year patent term. *See supra* note 129. Our goal was to identify a date on which it could reasonably be concluded the company had begun preclinical testing. But this period is a rough proxy for the preclinical testing period for at least two reasons. First, the preclinical testing will usually have usually begun *before* this filing date. *See supra* note 70. Second, the patent in question might not be the earliest filed patent or the active ingredient patent.

¹⁵³ The coefficient for this variable (length of the “proxy-preclinical” testing period) was negative but numerically low (-0.0018). In simple terms, the coefficient value represents how *much* of the dependent variable (here the effective patent life, measured in days) changes, with a one unit shift in the independent variable (here length of “proxy-preclinical” testing, measured in days), if the other independent variables are held constant. For the length of the clinical testing period, the coefficient was again low, -0.0016. The “p-values” for both independent variables — in simple terms the probability that the results occurred by chance — were below 0.000.

patent and patent term, with varying results. On the one hand, the following were positively correlated with effective patent life before restoration — very strong correlated: (1) a child patent, (2) a patent with a 17-year term because of the URAA transition provisions, (3) a patent with a 20-year term because of the URAA transition provisions, and (4) a patent with a post-URAA 20-year term were positively correlated with effective patent life. On the other hand (1) a child patent with a transitional 20-year term, and (2) a child patent with a post-URAA 20-year term were strongly negatively correlated with effective patent life before the restoration award. These findings are unsurprising and are discussed in section IV.

The number of days restored by PTO was negatively correlated with effective patent life before restoration. This makes sense, because the restoration award is based on the number of days lost. The coefficient was, however, quite small (-0.0017), meaning the impact was small. Imposition of the two-year cap on the restoration award was strongly negatively correlated with effective patent life (before restoration). The reasons for this are unclear but may relate to the fact that the two-year cap applied only to patents issued before September 24, 1984, covering drugs already in clinical trials. More than three quarters (86 of 113, or 76%) of these patents had been filed in the 1960s or 1970s, which suggests that the drugs in question had unusually long overall research and development programs.

2. Effective Patent Life After Patent Term Restoration

We performed five statistical regressions to assess which variables explain effective patent life *after* patent term restoration, that is, final effective patent life. Regression 2 included the full dataset, 642 observations, while Regressions 3 through 6 examined subsets of the data defined by patent term. We isolated these subsets to establish whether the determinants of effective patent life differ by patent term regime (pre-URAA, post-URAA, or transitional).

Regression 2 examined the determinants of final effective patent life in the entire dataset of 642 observations.¹⁵⁴ Regression 3 examined the determinations of final effective patent life in the subset of 314 observations with a 17-year patent term.¹⁵⁵ This comprises 65 subject to the pre-URAA patent term regime and 249 that received 17-year terms by operation of the URAA transition provisions. Regression 4 examined the determinants of effective patent life after patent term restoration in the subset of 328 observations with a 20-year patent term.¹⁵⁶ This comprises 150 subject to the

¹⁵⁴ This was a least squares regression analysis. Details can be found in the Appendix.

¹⁵⁵ This was a least squares regression analysis. Details can be found in the Appendix.

¹⁵⁶ This was a least squares regression analysis. Details can be found in the Appendix.

post-URAA patent term regime and 178 subject to 20-year terms by operation of the URAA transition provisions. Regression 5 examined the determinants of final effective patent life in the subset of 150 observations with a post-URAA 20-year patent term.¹⁵⁷ Regression 6 examined the determinants of final effective patent life in the subset of 95 observations to which the five-year cap applied.¹⁵⁸

The results appear in Table 1 in the Appendix. The key findings follow.

First, in Regression 2, which considered the entire dataset of 642 observations, the determinants of final effective patent life were virtually the same as the determinants of effective patent life before restoration — with the exception that one would expect: the number of days restored.¹⁵⁹ Thus a longer clinical period was associated with a shorter final effective patent life, as was a longer proxy-preclinical period, although here too the association was weak. Selecting a child patent subject to the post-URAA 20-year term had the most powerful negative influence on final patent life (but overall, selecting a patent subject to the 20-year term had a strongly positive impact). Selecting a patent subject to the transition provisions (i.e., a patent for which the more favorable of the two term calculations applied) had the most powerful positive influence on final effective patent life. The independent variables in this regression explained 77 percent of the variation in final effective patent life.

Second, in every regression, the length of the proxy-preclinical period and the length of the clinical period had negative explanatory power. That is, as these periods got longer, the final effective patent life (*after* patent term restoration) consistently got shorter. We expected this. And in each regression, again, the coefficients were small but strongly statistically significant — meaning that the impact was small but unlikely to be a matter of chance.¹⁶⁰ In every regression, other independent variables played a more powerful role in driving the final effective patent life — typically variables relating to the patent selected for restoration.

Third, therapeutic categories were generally not correlated with final effective patent life. There were a handful of exceptions. In Regression 2, antipsychotic drugs were negatively correlated with final effective patent life. In two subsets — (1) the subset of patents with a 20-year patent term (through

¹⁵⁷ This was a least squares regression analysis. Details can be found in the Appendix.

¹⁵⁸ This was a least squares regression analysis. Details can be found in the Appendix.

¹⁵⁹ Because the number of days restored is proportional to the number of days lost, it should be negatively correlated with effective patent life before patent term restoration and positively correlated with effective patent life after restoration.

¹⁶⁰ The coefficient for this variable (length of the “proxy-preclinical” testing period) was negative but numerically low (-0.0018). For the length of the clinical testing period, the coefficient was again low, -0.0016. The “p-values” for both independent variables were below 0.000.

the URAA *or* the transition provisions), and (2) the further subset of patents subject only to the post-URAA regime — analgesic drugs were strongly negatively correlated with effective patent life before restoration. But on the whole therapeutic categories associated with long clinical programs were not associated with shorter final effective patent life. We did not expect this result and discuss it in section IV.B.

Fourth, the results for child patents were complex but generally confirmed our instincts. We expected that selecting a child patent for restoration would be associated with longer final effective patent life when a 17-year patent term applied, but not when the 20-year term applied. As noted, selecting a child patent subject to the post-URAA 20-year term had a powerful, highly significant, negative influence on final effective patent life, both before restoration and with restoration. In the subset of 328 observations with patents that have a 20-year term (through the URAA *or* the transition provisions) — Regression 4 — having a child patent was somewhat negatively correlated with final effective patent life. In the subset of 314 observations with 17-year patent terms (through the pre-URAA law *or* the transition provisions) — Regression 3 — none of the child patent variables had explanatory power. This is also the case in Regression 5, which considered the subset of 150 observations with the post-URAA 20-year patent term (i.e., no transitional terms): having a child patent had no explanatory power. Finally, in the subset of 95 observations subject to the five-year cap — Regression 6 — having a child patent was negatively correlated with final effective patent life, but having a child patent with a 17-year transitional term or a 20-year term (whether through the URAA *or* the transition provisions) was strongly positively correlated with final effective patent life. We discuss these results in section IV.A.

3. Fourteen-Year Effective Patent Life

We performed two additional regressions with the entire dataset of 642 observations to answer the same question in a different way, focusing on variables that dictate whether a drug enjoys the full 14 years of effective patent life possible under section 156. In our dataset, 215 drugs (33.5%) reached the 14-year limit.¹⁶¹ Regression 7 sought to identify variables that

¹⁶¹ This is lower than the percentage reported by Beall for recently approved best-selling drugs. *See* Beall et al., *supra* note 26, at 21 (reporting that 31 drugs out of 83, or 37%, in the sample had restored patent life reaching the 14-year limit). When the 113 drugs subject to the 2-year cap are excluded from our dataset, 210 of the remaining 529 drugs (40%) hit the 14-year cap. This is much lower than the percentage reported by Beall. *See id.* (reporting that when drugs subject to the two-year cap were excluded from the analysis, the percentage rose to 70 (31 of 44 drugs). *See also* Congressional Budget Office, *supra* note 145, at 40

determine the percentage of 14 years achieved by a particular drug.¹⁶² Regression 8 sought to identify the variables that determine whether a drug comes close to reaching the 14-year limit — specifically, within 10 percent of 14 years — thus, whether the final effective patent life was 12.6 or more years.¹⁶³ Within our dataset, 334 drugs (52.0%) reached 12.6 years or more of final effective patent life.

In both regressions, the length of the proxy-preclinical testing period and the length of the clinical period had negative explanatory power. That is, as these periods got longer, the percentage of 14 years got shorter, and the chances of reaching at least 12.6 years got lower. But the actual impact was trivial. The independent variables selected for Regression 7 explained 77 percent of the variability in the percentage of 14 years achieved, and the most powerful determinants were — in order of decreasing influence: (1) selection of a patent that would enjoy 17 years through the transition provisions (positive), (2) selection of a patent under the new post-URAA patent regime (positive), (3) selection of a patent that would enjoy 20 years through the transition provisions (positive), (4) selection of a child patent subject to the 20-year term (negative), (5) selection of a child patent (positive), (6) selection of a child patent subject to the 20-year term through the transition provisions (negative), (7) application of the two-year cap (negative), and (8) selection of a child patent subject to a 17-year term through the transition provisions (negative). The antipsychotic therapeutic category also had explanatory power (negative). Regression 8 had low explanatory power, suggesting that omitted variables may have a fair amount to do with whether a drug hits at least 12.6 years.¹⁶⁴ These findings are discussed in section IV, and the full results appear in Table 2 in the Appendix.

IV. DISCUSSION

The findings in this study provide compelling support for some of the initial hypotheses and raise an interesting question about the impact of the 1994 change in the patent term.

(“about half of the 43 drugs introduced between 1992 and 1995 that received Hatch-Waxman extensions and were not limited by the transitional cap had their extensions limited by the 14-year cap”).

¹⁶² This was a least squares regression analysis. Details can be found in the Appendix.

¹⁶³ This was a probit regression. Details can be found in the Appendix.

¹⁶⁴ The adjusted R^2 was 0.65, meaning that only 65 percent of the variation in the dependent variable (here, whether the final term was 12.6 years or higher) is explained by the independent variables found to have explanatory power.

A. Distortion and Paradox

The primary incentive to discover and develop a new medicine is the prospect of a period for exclusive marketing made possible in part by the protection of patents associated with the medicine.¹⁶⁵ But by the time the federal government permits the inventor to commercialize the invention, much of the patent term has already lapsed. In the years before enactment of section 156, effective patent life for drugs had dropped to 9.5 years.¹⁶⁶ Many who supported patent term restoration — not only drug patent owners but FDA, PTO, and academic economists — grounded their arguments in this distortion, citing the length of premarket testing programs, the shortening of effective patent life, and concerns about the incentive to innovate.¹⁶⁷

Our legal system does not merely distort patents, however; it paradoxically provides less incentive (truncates the patent more) when a drug takes more time to develop. We call this the innovation paradox, and we hypothesized that it would be readily apparent when examining the drugs in our dataset before PTO extended their patent terms. And it was. Moreover, because the 1984 law does not restore every day of patent life lost to premarket research and development, we hypothesized that the paradox would still be evident today. And it is. The paradox was apparent in every regression considering the determinants of final effective patent life. In every regression, a longer clinical period was associated with a shorter final effective patent life, and a longer period between patent filing and clinical trials was associated with a shorter final effective patent life. Although the magnitude of the impact was very small, the results were strongly statistically significant, confirming our hypothesis that longer premarket research and development programs lead to shorter effective patent life, even with patent term restoration in place.¹⁶⁸

Our findings also show that the type of patent restored — child or parent, subject to the 17-year term or the 20-year term — has played a powerful role in determining final effective patent life. This merits reflection, because Congress chose in 1984 to allow companies to *select* the patent for restoration, and because it later amended the patent term *without* considering the effect of the change on patent term restoration.

¹⁶⁵ See *supra* section I.B.

¹⁶⁶ Eisman & Wardell, *supra* note 84, at 20.

¹⁶⁷ See generally Lietzan, *Political Economy*, *supra* note 80, at 111-125.

¹⁶⁸ In several regressions, specific years of marketing approval also had explanatory power. For instance, in Regression 2 (determinants of final effective patent life in the entire dataset), every year of FDA approval between 1985 and 2014, inclusive, was correlated with shorter effective patent life, with the coefficient varying from -1.76 (1985) to -4.14 (2010). This indicates that relative to the base year of 1984, patents on drugs approved in subsequent years had shorter final effective patent lives.

When Congress enacted patent term restoration in 1984, it assumed a simple world. The patent term lasted for 17 years from issuance. In August 1984 Senator Hatch and Representative Waxman brokered a series of final changes to the pending legislation, to secure the drug industry's support (and tacit agreement not to challenge an aspect of the legislation that raised constitutional issues).¹⁶⁹ Chief among these changes was the elimination of language that limited patent term restoration to the first-issued patent on the drug.¹⁷⁰ This language had reflected objections to the restoration of continuation patents,¹⁷¹ and its elimination would make it possible for a company to reach 14 years of effective patent life with a child patent.¹⁷² And that was the point.¹⁷³ It would be possible to reach 14 years with a child patent *because* of the 17-year patent term. In this simple world, if a patent issued after clinical trials began, less of the clinical period would be eligible for restoration.¹⁷⁴ If this patent was a child patent, though, it had a later original expiry date than earlier-issued patents, which meant that the smaller number of days would be added to a later original expiry date. And because PTO restored only 50 percent of the time spent in trials, restoring this later-issuing child patent would always mean a longer final effective patent life than restoring an earlier-issuing patent of either type.

Congress changed how patent terms would be calculated in 1995, and — simply as a mathematical matter — gutted the August 1984 decision. Once the URAA takes full effect — that is, once drug companies have *only* post-URAA patents from which to select — every patent that could be proposed for restoration will enjoy a 20-year term starting on its application date or its parent's application date. As already explained, a later-filed patent will generally issue later, so less of the clinical period will be eligible for restoration. But in this new world, if the later-filed patent is a child patent, it will *not* have a later original expiration date (to add this smaller restoration to). In other words, the company can no longer use a continuation patent to ensure it receives 14 years of final effective patent life — as envisioned in the final round of negotiations in 1984.

Our results, though complex, generally confirm this gutting. To begin with, selecting a child patent is positively associated with nearing the 14-year limit on effective patent life — *even though* selecting a child patent with a transitional term (of either sort) or a child patent with a 20-year term is

¹⁶⁹ Lietzan, *Political Economy*, *supra* note 80, at 105-106.

¹⁷⁰ Alfred B. Engelberg, *Special Patent Provisions for Pharmaceuticals: Have They Outlived Their Usefulness?*, 39 J. L. & TECH. 389, 404-405 (1999).

¹⁷¹ E.g., Lietzan, *Political Economy*, *supra* note 80, at 88.

¹⁷² *Id.* at 106.

¹⁷³ *Id.*

¹⁷⁴ See *supra* section II.

negatively associated (Regression 7). These findings provide powerful confirmation of the value of selecting a child patent in the remaining (alternative) scenario: when the pre-URAA 17-year term applied.¹⁷⁵ This is precisely what Congress intended in 1984. In contrast, selecting a child patent for restoration is associated with a shorter final effective patent life in the case of a child patent with a 20-year term, either through a transitional term or post-URAA (Regressions 1, 2, and 4). This is precisely the opposite of what Congress intended in 1984.¹⁷⁶

The nature of the patent term restoration formula makes it impossible to draw robust conclusions about the impact of the URAA using this dataset.¹⁷⁷ Although the URAA took effect in June 1995, and indeed applied in a sense retroactively (by applying transition provisions to patents then in force), in another sense *even now* it is not fully in place for the patent term restoration purposes. Only one-quarter of the restored patents in our dataset (150 patents, or 23%) were post-URAA patents. And in this subset, none of the patent-related independent variables has explanatory power. Only 65 patents in the dataset (10%) were subject to the pre-URAA scheme.¹⁷⁸ A comparison of

¹⁷⁵ In Regression 7, which uses the full set of 642 observations to examine the percent of the 14 years achieved, selecting a child patent with a transitional 17-year term was negatively associated with nearing the 14-year limit. Such a patent would be assigned the 17-year term simply because applying the 20-year term was less advantageous. This would be true — the old calculation would have been more favorable — if the parent application had been filed more than 3 years before PTO issued the child patent. It is possible the lapse of time between parent and child applications reflects a longer overall premarket research and development process, which could help to explain the negative association with getting close to 14 years. But we did not test this in our regressions.

¹⁷⁶ Regression 5 complicates the picture. This considered the determinants of final effective patent life in the 150 observations subject to the post-URAA patent term, and it found that a child patent had no explanatory power. This likely reflects the fact that section 156 allows a company to *select* any patent for restoration. In the pre-URAA period, a company could *choose* a child patent in order to achieve 14 years. Although this strategy is unlikely to work in the post-URAA world, the company would presumably avoid selecting a child patent that would work to its disadvantage.

¹⁷⁷ The text addresses whether the URAA eliminated the intended benefit of selecting a child patent for restoration. The URAA could have had *another* negative impact on effective patent life, but enactment of patent term adjustment — applicable to patent applications filed after May 29, 2000 — should have offset that impact as follows. The URAA would ordinarily lead to shorter effective patent life than prior law if a patent application was pending at PTO for more than three years, because in this case 20 years from the application would end earlier than 17 years from issuance. When patent term adjustment applies, however, delay beyond the three years is generally added back day for day. *See supra* note 117. Suppose the patent issues during the clinical trials. The company may seek patent term restoration for all days in trials after patent issuance, though it will be limited to 50 percent recovery. If the patent was delayed at the PTO, it may *also* recover those days, but it will receive them in full.

¹⁷⁸ The vast majority of the patents in our dataset — 427 patents, or 68% — were subject

the average final effective patent life in the two groups — 12.48 years for post-URAA patents and 7.36 years for pre-URAA patents — would not tell us the impact of the URAA, because 74% of the pre-URAA patents were also subject to the two-year cap, which no longer applies. In an attempt to better understand the impact of the URAA, however, we recalculated patent term restoration in the counterfactual world in which Congress did not change the patent term and did not enact patent term adjustment.¹⁷⁹ In this counterfactual world, the average effective patent life in our dataset after restoration would have been 11.61 years, which is not meaningfully different from the average in the real world (11.58 years).¹⁸⁰

Within a few years, every company with a recently approved drug or biologic will hold only patents subject to the 20-year term.¹⁸¹ At this point, it will no longer be possible to obtain 14 years of effective patent life on a continuation patent through application of patent term restoration. A very short research and development program will always have the potential to yield 14 years of effective patent life. Otherwise the path to a 14-year effective patent life will be different: use of a later-issued original patent.¹⁸² But whether this patent will effectively preclude approval and launch of a generic or biosimilar copy is another question.¹⁸³ These are issues that Congress did not consider in 1995. A review of the legislative history suggests no attention was paid to the relationship between the new patent term and the formula for patent term restoration.¹⁸⁴

to the URAA transition rules.

¹⁷⁹ This counterfactual has limitations. For instance, we changed no other variables and thus assumed that PTO took the same amount of time to issue the patent. We also assumed the company would have selected the same patent for restoration.

¹⁸⁰ The median would have been higher (13.05 years, instead of 12.83 years).

¹⁸¹ Only one of the six drugs in our dataset approved by FDA in 2015 — the latest year for which we have data — had a transition patent restored. Only two of the 13 approved in 2014 had a transition patent restored. And although our study does not cover new drugs approved in subsequent years, only two new chemical entities approved in 2018 are covered by composition of matter or method of use patents with transitional terms.

¹⁸² This could explain why the results in the counterfactual world are not meaningfully different from the results in the real world. So long as PTO issued those original patents within three years of the patent application, the initial and restored patent expiry dates would not have been significantly different had the pre-URAA regime applied.

¹⁸³ These will not be active ingredient patents, which are the most likely to block approval of an abbreviated application. *See supra* section I.B.; *see also* Henry Grabowski et al., *Pharmaceutical Patent Challenges: Company Strategies and Litigation Outcomes*, 3 AM. J. HEALTH ECON. 33, 40 (2017) (“Most often, firms will then apply for patent term extension on their key active ingredient patent, since this provides the broadest scope of patent protection and frequently expires earlier than any non-AI patents.”).

¹⁸⁴ Although policymakers may have discussed the relationship between the URAA and patent term restoration, we found no evidence of these discussions in the following legislative materials: Uruguay Round Agreements Act; H. Rep. No. 826, Pt. 1 (Oct. 3, 1994);

B. Role of Therapeutic Category

Uruguay Round Agreements Act; H. Rep. No. 826, Pt. 2 (Oct. 3, 1994) Providing for Consideration of H.R. 5110; H. Rep. No. 829 (Oct. 4, 1994); Uruguay Round Agreements Act; S. Rep. No. 412 (Nov. 22, 1994); H.R. Doc. No. 195, 103d Cong., 2d Sess. (1994); H.R. Doc. No. 316, 103d Cong., 2d Sess., Vol. 1, (1994); H.R. Doc. No. 316, 103d Cong., 2d Sess., vol. 2 (1994); 140 Cong. Rec. (all dates, both House and Senate); Uruguay Round of Multilateral Trade Negotiations: Hearings before the Subcomm. on Trade of the Committee on Ways and Means in the House of Representatives, 103d Cong., 1st Sess., (1993); Trade Agreements Resulting from the Uruguay Round of Multilateral Trade Negotiations: Hearings before the Comm. on Ways and Means and Its Subcomm. on Trade in the House of Representatives, 103d Cong., 2d Sess., (1994); GATT: The Experts View: Hearing before the Subcomm. on Economic Policy, Trade and Environment of the Comm. on Foreign Affairs in the House of Representatives, 103d Cong., 2d Sess., (1994); Review of the Uruguay Round GATT Agreement Implications for Agricultural Trade: Hearings before the Comm. on Agriculture in the House of Representatives, 103d Cong., 2d Sess., (1994); Uruguay Round of Multilateral Trade Negotiations: Hearing before the Subcomm. on Commerce, Consumer Protection, and Competitiveness of the Comm. on Energy and Commerce in the House of Representatives, 103d Cong., 2d Sess. (1994); GATT Subsidies Code and Its Impact on R&(and)D: Hearing before the Subcomm. on Technology, Environment and Aviation of the Comm. on Science, Space, and Technology in the House of Representatives, 103d Cong., 2d Sess. (1994); World Trade Organization: Hearing before the Comm. on Ways and Means in the House of Representatives, 103d Cong., 2d Sess. (1994); Uruguay Round of Multilateral Trade Negotiations: Hearing before the Comm. on Finance in the Senate, 103d Cong., 1st Sess., (1994); General Agreement on Tariffs and Trade: Hearing before the Comm. on Labor and Human Resources in the Senate, 103d Cong., 2d Sess. (1994); Results of the Uruguay Round Trade Negotiations: Hearings before the Comm. on Finance in the Senate, 103d Cong., 2d Sess., (1994); GATT Implementing Legislation: Hearings before the Comm. on Commerce, Science, and Transportation in the Senate, 103d Cong., 2d Sess., (1994); Staff of the Joint Comm. on Taxation, 103d Cong., 2d Sess., Description of the Chairman's Mark Relating to the Financing Options for Implementing the Uruguay Round Agreement of the General Agreement on Tariffs and Trade (GATT), (Comm. Print 1994); Staff of the Joint Comm. on Taxation, 103d Cong., 2d Sess., Possible Proposals to Finance the Uruguay Round Agreement of the General Agreement on Tariffs and Trade, (Comm. Print 1994); Staff of the Joint Comm. on Taxation, 103d Cong., 2d Sess., Descriptions of Proposals Relating to Financing the Implementation of the Uruguay Round Agreement of the General Agreement on Tariffs and Trade (GATT) as Approved by the Senate Committee on Finance, (Comm. Print 1994); Staff of the Joint Comm. on Taxation, 103d Cong., 2d Sess., Estimates of Financing Package for the Uruguay Round Agreement of the General Agreement on Tariffs and Trade, (Comm. Print 1994); Staff of the Joint Comm. on Taxation, 103d Cong., 2d Sess., Staff Recommendations for Tentatively Agreed to Items in Financing Package for the Uruguay Round Agreement of the General Agreement on Tariffs and Trade, (Comm. Print 1994); Staff of the Joint Comm. on Taxation, 103d Cong., 2d Sess., Summary of the Provisions for Financing the Implementation of the Uruguay Round of the General Agreement on Tariffs and Trade (GATT) (Comm. Print 1994); Staff of the Joint Comm. on Taxation, 103d Cong., 2d Sess., Financing Provisions for the Uruguay Round Agreement of the General Agreement on Tariffs and Trade (GATT) (Comm. Print 1994).

We expected that some therapeutic categories would be associated with shorter effective patent life. Studies before enactment of section 156 had noted that effective patent life varied by therapeutic category,¹⁸⁵ but the policymaking discussions related to design of section 156 did not take this into account.¹⁸⁶ Clinical program length has continued to vary by therapeutic category.¹⁸⁷ Because the formula did not take this possibility into account, and because it does not restore every day of patent life lost to premarket research and development, we expected that therapeutic categories would be associated with shorter effective patent life both before and after restoration.

The therapeutic categories in our dataset vary in effective patent life without restoration: from an average of 4.51 years (eight antipsychotics) to an average of 11.91 years (six antimigraine agents). In addition to antipsychotics, sleep disorder agents, anticonvulsants, vaccines, analgesics, and antidepressants average seven or fewer years of effective patent life remaining at the time of FDA approval. In addition to antimigraine agents, antivirals, diagnostic agents, dermatological agents, and anesthetics average ten or more years of patent life remaining. Most categories had large ranges. For instance, antibacterials ranged from -0.76 years to 13.86 years; antidepressants ranged from -1.5 years to 13.96 years, and cardiovascular drugs ranged from -2.7 years to 13.8 years. Final effective patent life *after* restoration varies less by therapeutic category (as it does less in general), ranging again from antipsychotics (8.29 years) and sleep disorder agents (9.61 years) at the low end to antiviral drugs (13.18 years) and antimigraine agents (13.74 years) at the high end. Final effective patent life still varies within each category; antibacterials, for instance, range from 3.69 years to the full 14 years. These results appear in Table 3 in the Appendix.

Although effective patent life — before and after restoration — varies by therapeutic category, our regressions showed that therapeutic category generally does not explain effective patent life. As noted, there were a few exceptions, but the explanatory power is not strong, and the statistical significance is not overwhelming.¹⁸⁸ This may stem from the small number of observations in each therapeutic category, limiting the category's explanatory power. But the value of the therapeutic category for empirical

¹⁸⁵ E.g., Leonard G. Schiffrin, *Lessons from the Drug Lag: A Retrospective Analysis of the 1962 Drug Regulations*, 5 HARV. J. L. & PUB. POL'Y 91, 116 (1982) (showing the decline in average effective patent life from 1966-69 to 1970-73 by therapeutic area, and showing that diuretics and cardiovascular drugs and anti-inflammatory agents were the hardest hit) (citing Schwartzman, *supra* note 84).

¹⁸⁶ See generally Lietzan, *Political Economy*, *supra* note 80 (providing history of the Hatch-Waxman Amendments, including section 156, based on exhaustive review of the legislative history).

¹⁸⁷ See *supra* note 58.

¹⁸⁸ See *supra* section III.C.2.

scholarship relating to innovation policy continues to be unclear. Therapeutic categories generally group drugs by body system or symptom targeted, rather than by disease or condition targeted, type of condition (acute or chronic), chemical class, mechanism of action, or physiological effect.¹⁸⁹ As a result, many categories contain drugs that have in common *only* the body system targeted. Some categories are wildly variable in both clinical trial length and effective patent life, suggesting that therapeutic category might *not* be the correct way to understand the effect of patent term distortion. It is convention in innovation policy to work by therapeutic category, but when focusing on the effect of research and development challenges and regulatory requirements, it may be more appropriate to focus on pharmacologic class instead.¹⁹⁰ We did not capture this in our dataset.

C. Impact of the Five-Year and Two-Year Caps

Earlier work led us to suspect that the five-year cap exacerbates the distortion of patents by the regulatory framework. The cap means that once a clinical program reaches a certain length, any more testing will simply translate to lost patent life. We hypothesized that hitting the five-year cap would make a drug's final effective patent life shorter and less likely to reach the 14-year limit.

The results were more nuanced. Application of the five-year cap had no explanatory power with respect to final effective patent life in the entire dataset (Regression 2) or the subset of observations with a 17-year patent term (Regression 3), nor did it explain the percentage of 14 years attained by a patent owner in the full dataset (Regression 7). But in the subset with a 20-year patent term (Regression 4) and the subset with a post-URAA 20-year patent term (Regression 5) — subsets presumably more relevant to the impact of the scheme going forward — application of the five-year cap variable was modestly correlated with shorter final effective patent life. In addition, application of the five-year cap is negatively correlated with reaching at least 12.6 years. That is to say, application of the five-year cap results in the final effective patent life being less likely to fall within 10 percent of the maximum possible 14 years. And although the coefficient is small, the results are strongly statistically significant — which means that the impact is minor but unlikely to be a matter of chance.¹⁹¹ No drug in the dataset that hit the five-year cap secured 14 years of effective patent life.

¹⁸⁹ Littman, *supra* note 46, at 22; FDA, PAVING THE WAY FOR PERSONALIZED MEDICINE 17 (Oct. 2013).

¹⁹⁰ E.g., Lietzan, *Innovation Paradox*, *supra* note 39, at 105-06 (finding less variability in average clinical program length when drugs are classified by pharmacological class).

¹⁹¹ The coefficient for this variable is -1.3181, and the p-value is below 0.000.

Interpretation of these results is complicated by the fact that more drugs in the dataset were subject to the two-year cap for transitional patents than the currently applicable five-year cap. Within our dataset of 642 drugs, 95 (15%) hit the five-year cap.¹⁹² (These drugs had an average effective patent life of 5.19 years before restoration and 10.20 years after restoration, lower than the overall population averages.) But if a product was already in clinical trials on September 24, 1984, then a patent issued before that date could receive no more than two years of patent term restoration. This transition provision turned out to apply to 113 drugs — 18 percent of the dataset — including drugs approved well into the 1990s and indeed one approved in 2000.¹⁹³

Imposition of the transitional two-year cap has two implications. First, it means the discussion above understates the percentage of drugs likely to be affected by five-year cap going forward. In a counterfactual world in which Congress included only the five-year cap, 151 drugs (24% of the dataset) would have been subject to that cap. These drugs would have had a final effective patent life of 9.97 years. Second, imposition of the two-year cap was negatively correlated with effective patent life in every regression in which the variable had explanatory power. This means it drives down effective patent life, so the average final effective patent life reported in this study — 11.58 years for the entire dataset — is lower than it would have been if only *current* law (the five-year cap) had applied. Had only the five-year cap applied, the dataset would have had an average final effective patent life of 11.96 years (median 13.16). In this world, the average final effective patent life for the 24% of drugs subject to the cap (9.97 years) would have been meaningfully shorter than the population average.

D. Actual Exclusivity in the Market

The findings in this Article relating to effective patent life will be important for scholars and policymakers focusing on drug innovation policy, but they are subject to one cautionary note. As opponents of patent term restoration pointed out in the late 1970s and early 1980s, effective patent life (of one patent, among many) is different from actual exclusivity in the market.¹⁹⁴ Actual exclusivity is the time before launch of a generic copy (or

¹⁹² This is consistent with Beall's findings. Beall, *supra* note 26, at 21 (reporting that 13 of 83 drugs, or 15%, hit the 5-year cap). When the drugs that hit the 2-year cap are excluded from the analysis, however, 18 percent of the remaining drugs in our dataset (95 of 529) hit the 5-year cap, compared to 30 percent (13 of 44) in Beall's dataset. *Id.*

¹⁹³ This was Mifeprex (mifepristone), approved by FDA for termination of early pregnancy in September 2000.

¹⁹⁴ *E.g.*, Lietzan, *Political Economy*, *supra* note 80, at 83-84 (noting that when drug

a biosimilar, for a biologic). This period could be shorter than the effective life of the patent as reported in this dataset — for instance, if the restored patent is later invalidated, or if patent infringement litigation leads to a settlement allowing the generic company to launch before patent expiry. It could be shorter if it is possible for a generic company to satisfy the generic drug approval standard *without* infringing the patent — which might be the case, for example, if the patent selected for restoration covers the dosage form, formulation, or manufacturing process.¹⁹⁵ Actual exclusivity could also be longer than the effective patent life reported in this dataset.¹⁹⁶ It could be longer if the market for the drug is too small to attract generic competitors. It could be longer if the drug is difficult (or expensive) to make, or too complex for proposed copies to meet the generic drug approval standard (which requires a showing that the active ingredients of the two drugs are the same). Or there could be other intellectual property effectively preventing generic competition, including later-expiring patents.

We calculated the actual market exclusivity period — meaning the time from new drug approval to generic drug launch — for 227 of the 554 drugs in the dataset.¹⁹⁷ Generic drug launch in this context means launch of a generic drug containing the same active ingredient, even if the generic drug approval was based on a different innovative product containing the same ingredient.¹⁹⁸ The average exclusivity period was 12.62 years (median 13.28). This matches the findings of earlier studies.¹⁹⁹ Another 265 drugs

patent owners pushed for patent term restoration in the late 1970s and early 1980s, opponents such as Public Citizen argued that shortened effective patent life was irrelevant, because it did not correspond with actual exclusivity in the market).

¹⁹⁵ FDA will approve a generic drug if it has the same active ingredient, route of administration, dosage form, strength, and labeling as its reference product, and if it is bioequivalent to that reference product. 21 U.S.C. § 355(j)(4). In addition, if the agency has approved a special petition (known as a “suitability petition”) from the generic manufacturer, it will approve a generic copy with a different route of administration, dosage form, or strength. *Id.* § 355(j)(2)(A)(iii). It does not compare the manufacturing methods. Nor does the formulation have to be the same, although in some cases FDA will require the same inactive ingredients in the same concentration. E.g., 21 C.F.R. § 314.94(a)(9).

¹⁹⁶ See, e.g., Comments of the Association for Accessible Medicines, Docket No. FDA-2017-N-3615 (Nov. 17, 2017), at 7-9 (describing a variety of factors considered by generic companies when deciding whether to pursue a generic copy of a drug that has no patent protection).

¹⁹⁷ IQVIA provided the launch dates. See *supra* note 141. For 265 drugs, IQVIA reported no generic launch to date. As explained in note 141, we dropped another six drugs because the dates were not useable in our analysis and 56 drugs for which IQVIA lacked data.

¹⁹⁸ This was necessary because the IQVIA data did not identify the innovative product on which the generic drug was based.

¹⁹⁹ E.g., Beall et al., *supra* note 26, at 20 (reporting average exclusivity in the market — time to generic market entry — as 13.75 years for 83 top-selling drugs, identify the quarter

had no generic launch as of the date we concluded data collection. Although it is tempting to consider the number of years since their FDA approval as their effective market exclusivity, many — such as Posicor (mibefradil dihydrochloride), Normiflo (ardeparin sodium), Rezulin (troglitazone), and Manopax (flosequinan) — were withdrawn from the market, including some for safety reasons (meaning that no generic could ever be approved).²⁰⁰ The numbers of years since FDA approval of these drugs cannot be construed as their effective market exclusivity.

We performed three regressions to identify the determinants of actual market exclusivity. Regression 9 considered all 227 drugs for which we have generic launch data, Regression 10 considered the subset of 131 drugs with 17-year patent terms, and Regression 11 considered the subset of 96 drugs with 20-year patent terms. The results appear in Table 4 in the Appendix. Regressions 10 and 11 had no explanatory power and are not discussed further. In the 227 drugs for which we have generic launch data, the final effective patent life after restoration is positively associated with actual market exclusivity (coefficient 0.44, $p=0.024$), as is the number of days of patent life restored (but the coefficient here is small). These were the only independent variables with explanatory power, and they explain only 22 percent of the variation in actual market exclusivity.²⁰¹

Whether effective patent life corresponds to actual market exclusivity is important, but focusing on actual market exclusivity may miss the point. The distortion of drug patent life by federal regulatory requirements raises concerns because our legal system uses the *promise* of patent protection to encourage the discovery and development of new medicines.²⁰² Even if the life of the restored patent turns out — in the end — not to dictate the timing

of generic market entry as the one in which a prescription for a therapeutically equivalent generic drug appeared in Medicaid prescription data aggregated by the Centers for Medicare and Medicaid data Bo Wang et al., *Research Letter: Variations in Time of Market Exclusivity Among Top-Selling Prescription Drugs in the United States*, 175 JAMA INT. MED. 635 (2015) (finding median market exclusivity period of 12.5 years for the 175 drugs that experienced generic competition by the end of 2012, out of the 437 top-selling drugs by sales in the United States between 200 and 2011, also using Medicaid prescription data as proof of generic competition); Henry Grabowski et al., *Recent trends in brand-name and generic drug competition*, 17 J. MED. ECON. 207 (2014) (finding that non-biologic drugs experiencing initial generic entry in 2011-2012 had enjoyed 12.9 years of actual exclusivity in the market, using IQVIA data to confirm generic launch).

²⁰⁰ We did not attempt to identify every drug withdrawn from the market.

²⁰¹ Wang and colleagues found that median market exclusivity differed by therapeutic area, ranging from 14.8 years (dermatology products and antivirals) to 8.0 (analgesics). Wang, *supra* note 199, at 636.

²⁰² See *supra* section I.B. Patent protection provides this encouragement because it is designed to prevent competitors from making, using, or selling the invention for a fixed time period. 35 U.S.C. § 271(a).

of actual generic launch, when a company is starting clinical trials — in our dataset, an average of 19.58 years *before* the final (restored) patent expiry — the factors affecting market exclusivity may be unknown and actual market exclusivity impossible to predict. (The company does not even know whether the trials will succeed, and in fact chances are the trials will *not*.²⁰³) Patent life is more certain; when one applies for a patent, one generally knows (subject to delay at PTO and patent term adjustment) what the expiration date will be. Even though a company does not know how long its clinical program will take, it knows that *if* the drug is approved, it will have whatever remains of the patent life plus as many as five more years to make up for time lost to research and development. Potential effective patent life is thus more likely to be driving investment decisions at the beginning of the 19.58 years than is speculation about actual market exclusivity.

CONCLUSION

The findings in this Article have significant policy implications. Longer clinical programs lead to shorter effective patent life, even after patent term restoration has been awarded. Although the impact is small, even a modest impact could be financially significant for an innovator. This finding contributes to a growing body of literature asking whether the U.S. legal system may be systematically skewing drug research incentives away from research programs that require a substantial investment of time. The decision to limit recovery to 50 percent of the days in clinical trials and, perhaps more importantly, to cap recovery at 5 years, may warrant reexamination.

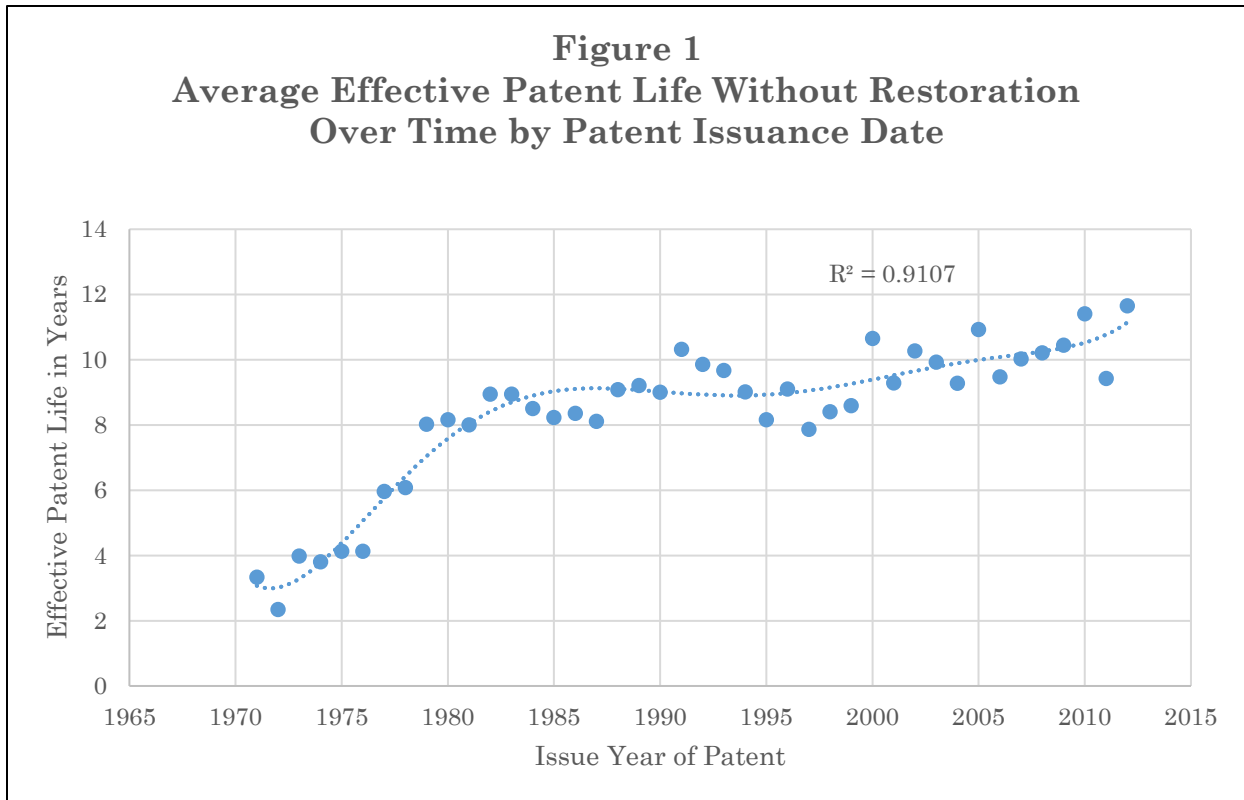
Other policy implications relate to the changes made to the patent term in 1994. Lawmakers in 1984 made a conscious choice to permit restoration of continuation patents so that drug companies could achieve 14 years of effective patent life under section 156. The ability to choose a later-issued child patent helped mitigate the distorting effect of the premarket regulatory regime. This was possible because the patent term was calculated from patent issuance. Lawmakers in 1994 changed how the patent term was calculated, and now a child patent is less likely to reach 14 years. The decision to unravel the choice made in 1984 — if a conscious decision was even made — was not vetted publicly. The consequences could be profound.

Under the changes made in 1994, a drug company may need to select a later-issued *original* patent to achieve the same result: 14 years of effective patent life. This patent is unlikely to cover the drug's active ingredient; instead it may cover another aspect of the drug such as its formulation. These patents may be inherently less valuable to the drug's inventor, because it may

²⁰³ See *supra* note 54.

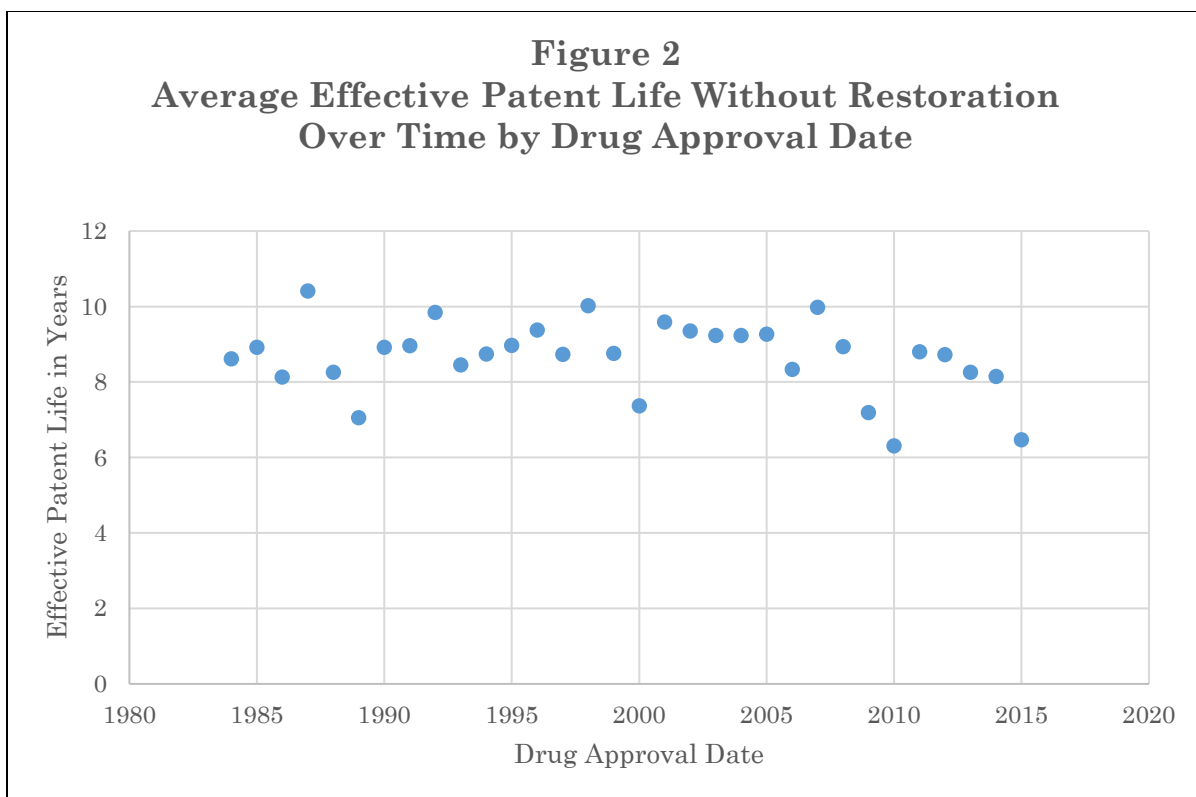
be possible for generic and biosimilar applicants to develop copies that satisfy regulatory requirements for copies and yet do not infringe the patent. If these patents do *not* have the same value, the 14 years of effective patent life is illusory. Policymakers effectively nullified the decision from 1984 without meaningful public discussion of the implications for drug innovation — discussion that is therefore overdue. If instead these patents *do* preclude approval of generic and biosimilar applications, their use in this fashion is fully consistent with the intent of Congress in 1984, and public rhetoric about the insidious nature of later-issued drug patents should be recalibrated.

APPENDIX



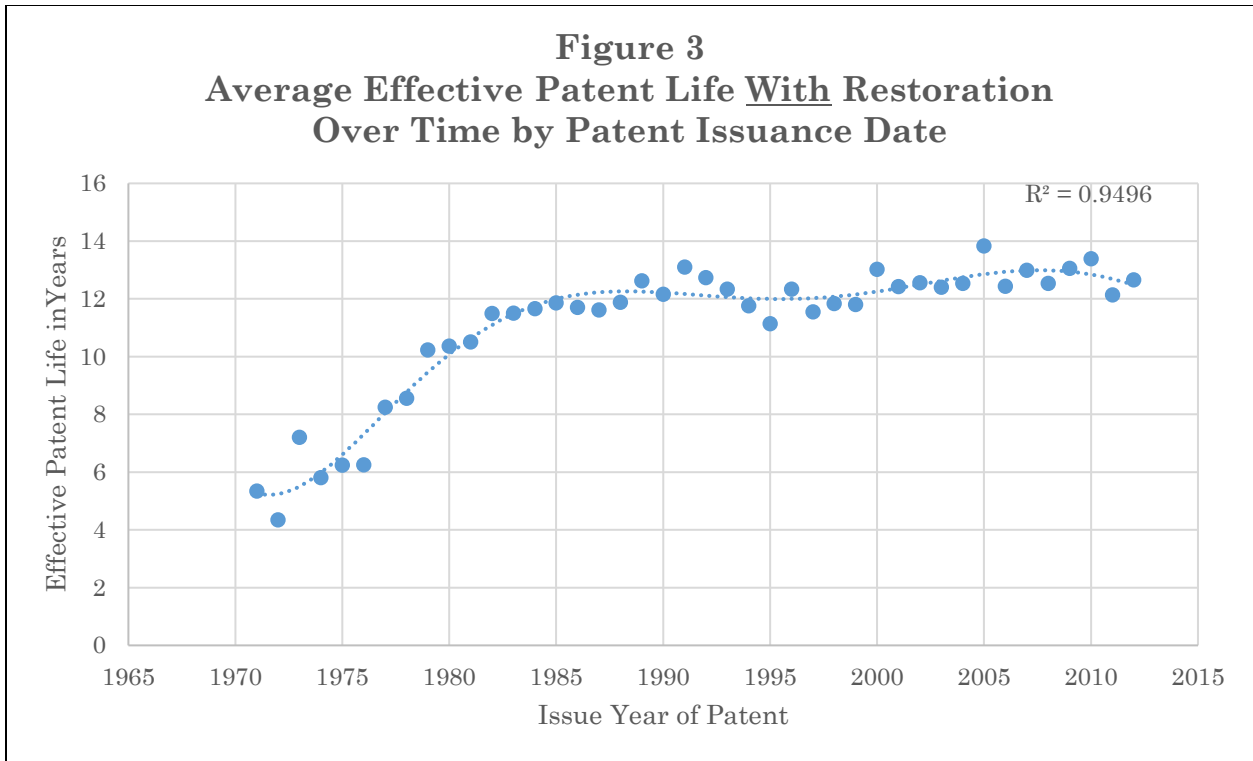
Notes:

- Some drugs had negative effective patent life before restoration. To generate this figure, all negative values were replaced with zero.
- There is a potential for selection bias at the beginning and end of the interval studied, as follows.
First, section 156 of the Patent Act did not take effect until September 1984, and the earliest approved drug in the dataset received FDA approval in August 1984. Any patent term restoration request relating to a patent issued in the 1970s necessarily related to a drug approved in August 1984 or later. These patents would have had an exceptionally short effective patent life. And other drugs with patents issued in the 1970s that reached the market more quickly will not appear in the dataset, because the earliest approved drugs were approved in August 1984. The information for these early patent issuance years will be skewed to suggest a shorter than warranted average effective patent life. The steep slope at the beginning of the interval studied is likely an artifact of enactment in 1984.
Second, there may also be skewing in the final years of patent issuance. If a patent issued in the early 2010s and covers a drug that appears in our dataset, it necessarily covers a drug approved before November 2015. Meanwhile, other patents issued in the early 2010s will not appear in the dataset if the drugs in question are still in development. The information for these later patent issue years will be skewed to suggest a longer than warranted average effective patent life.



Notes:

- Some drugs had negative effective patent life before restoration. To generate this figure, all negative values were replaced with zero.



Notes:

- As was true of Figure 1, and for the same reasons, there is a potential for selection bias for patents issued in the earliest years shown and patents issued in the latest years shown.

Figure 4
Average Effective Patent Life With Restoration
Over Time by FDA Approval Date

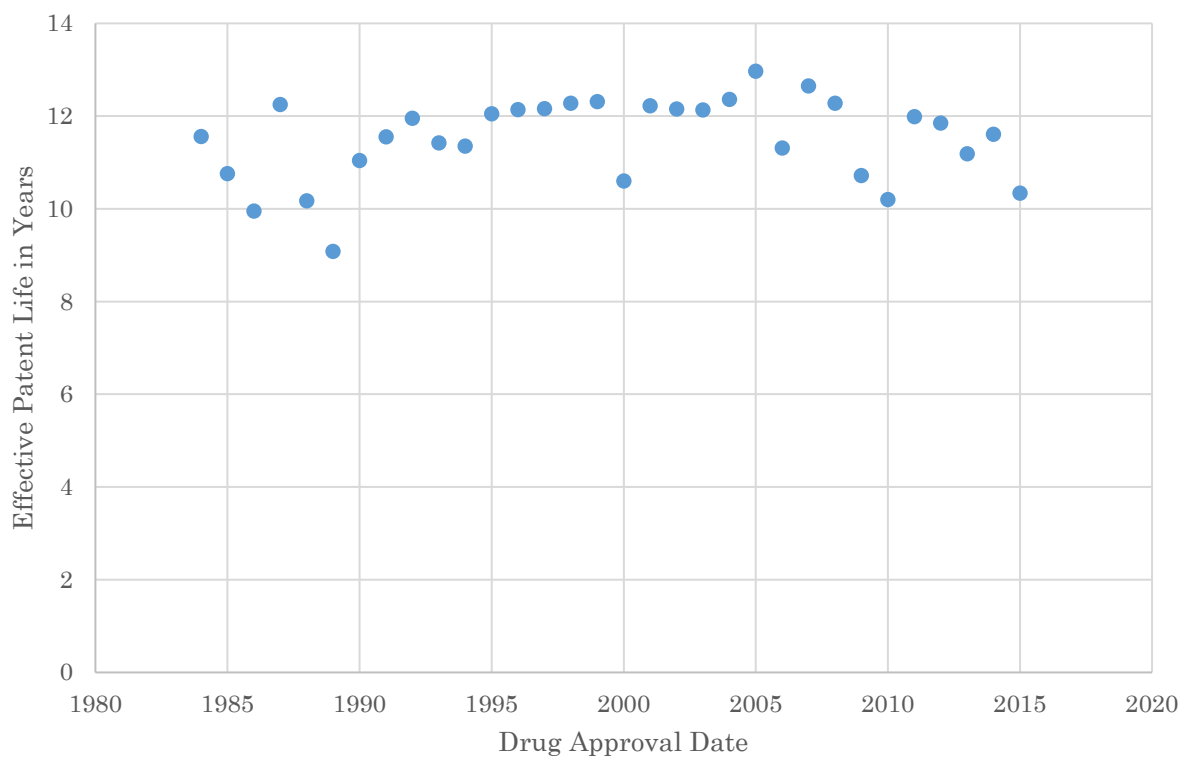


Table 1
Determinants of Effective Patent Life Before Patent Term Restoration and With Restoration

	Regression 1	Regression 2	Regression 3	Regression 4	Regression 5	Regression 6
Dependent variable	Effective patent life before restoration	Effective patent life with restoration	Effective patent life with restoration when the patent had a 17-year term (pre-URAA or transitional)	Effective patent life with restoration when the patent had a 20-year term (post-URAA or transitional)	Effective patent life with restoration when the patent is subject to the post-URAA 20-year term	Effective patent life with restoration when the 5-year cap applies
Observations	642	642	314	328	150	95
Adjusted R ²	0.84	0.77	0.75	0.90	0.78	0.68
Child patent	1.5228*** (0.41)	1.5245*** (0.41)	1.9131 (1.94)	2.4726* (0.89)	0.3999 (0.20)	-6.0061** (2.24)
Child patent with transition 17-year term	-0.8360 (0.47)	-0.8459 (0.47)	-1.6213 (1.97)	Omitted	Omitted	7.0480** (2.23)
Child patent with transition 20-year term	-1.4522** (0.48)	-1.4518* (0.48)	Omitted	-2.2139* (0.92)	Omitted	6.3905** (2.06)
Child patent with post-URAA 20-year term	-2.0196*** (0.49)	-2.0418*** (0.49)	Omitted	-2.9276*** (0.90)	Omitted	5.1669* (2.34)
Length of clinical testing period	-0.0016*** (0.00)	-0.0016*** (0.00)	-0.0011*** (0.00)	-0.0024*** (0.00)	-0.0021*** (0.00)	-0.0021*** (0.00)
Length of proxy preclinical period	-0.0018*** (0.00)	-0.0018*** (0.00)	-0.0014*** (0.00)	-0.0024*** (0.00)	-0.0021*** (0.00)	-0.0017*** (0.00)
Patent with transitional 17-year term	3.5268*** (0.43)	3.5289*** (0.43)	4.1121*** (0.56)	Omitted	Omitted	Omitted
Patent with transitional 20-year term	2.4389*** (0.39)	2.4436*** (0.49)	Omitted	-0.1909 (0.22)	Omitted	Omitted
Patent with post-URAA 20-year term	2.9172*** (0.49)	2.9256*** (0.49)	Omitted	Omitted	Omitted	Omitted
Application of 2-year cap	-1.3169*** (0.29)	-1.3231*** (0.29)	-1.5077* (0.52)	-0.6874** (0.26)	Omitted	Omitted
Application of 5-year cap	-0.4393 (0.23)	-0.4146 (0.23)	-0.2030 (0.42)	-0.3740* (0.18)	-0.7238* (0.36)	Omitted
Number of days restored	-0.0017*** (0.00)	0.0010*** (0.00)	0.0005 (0.00)	0.0020*** (0.00)	0.0016*** (0.00)	-1.8183 (2.24)
Therapeutic categories	Antipsychotic -1.3127* (0.64)	Antipsychotic -1.3135* (0.64)		Analgesics -1.3825** (0.47)	Analgesics -2.5909* (0.85)	

Notes:

- Estimated coefficients are given with standard errors in parentheses underneath. Variables are identified as having explanatory power as follows: * $p < .05$, ** $p < .01$, *** $p < .001$.
- Linear regression attempts to model the relationship between two variables by fitting a linear equation to observed data. This study utilizes a multivariate ordinary least squares (OLS) regression, a statistical method of analysis, in order to estimate the relationship between a dependent variable and a collection of independent variables. The regressions used in this analysis were:
 - Regression 1: In this OLS regression the dependent variable is the effective patent life before restoration. The independent variables are listed in the second column of Table 1.
 - Regression 2: In this OLS regression the dependent variable is the effective patent life with restoration. The independent variables are listed in the third column of Table 1.
 - Regression 3: In this OLS regression the dependent variable is the effective patent life with restoration when the patent had a 17- year term (pre-URAA or transitional). The independent variables are listed in the fourth column of Table 1. Since the regression examines only patents that had a 17-year term, all variables associated with a 20-year term are omitted. In addition, none of the therapeutic categories were found to have any explanatory power.
 - Regression 4: In this OLS regression the dependent variable is the effective patent life with restoration when the patent has a 20-year term (post-URAA or transitional). The independent variables are listed in the fifth column of Table 1. Since the regression examines only patents that had a 20-year term, all variables associated with a 17-year term are omitted. In addition, in this subset of the data, since patents with post-URAA 20-year term is perfectly correlated with patents with transitional 20-year term, only one of the two variables can be included in the regression. Accordingly, the variable, patent with post-URAA 20-year term, is omitted.
 - Regression 5: In this OLS regression the dependent variable is the effective patent life with restoration when the patent is subject to the post-URAA 20-year term (i.e., no transitional terms). The independent variables are listed in the sixth column of Table 1. Given the relatively small sample size in this regression (150 observations), several variables were omitted due to their lack of explanatory power and correlation with other variables.
 - Regression 6: In this OLS regression the dependent variable is the effective patent life with restoration when the 5-year cap applies. The independent variables are listed in the last column of Table 1. Given the relatively small sample size in this regression (95 observations), several variables were omitted due to their lack of explanatory power and correlation with other variables.

Table 2
Determinants of Effective Patent Life With Restoration

	Regression 7	Regression 8
Dependent variable	Percent of 14 Years Achieved	Whether the Final Effective Patent Life Was ≥ 12.6 years
Observations	642	629
Adjusted R ²	0.77	0.65
Child patent	10.8896*** (2.95)	1.1862 (1.49)
Child patent with Transition 17-year term	-6.0421* (3.38)	-0.7505 (1.54)
Child patent with Transition 20-year term	-10.3699** (3.45)	-1.06 (1.54)
Child patent with post-URAA 20-year term	-14.5841*** (3.50)	-2.5403 (1.54)
Length of clinical testing period	-0.0116*** (0.00)	-0.0010*** (0.00)
Length of proxy-preclinical testing period	-0.0130*** (0.00)	-0.0014*** (0.00)
Transitional 17-year term	25.2066*** (3.06)	3.1591* (1.50)
Transitional 20-year term	17.4546*** (2.81)	1.9636 (1.45)
Post-URAA 20-year term	20.8978*** (3.52)	2.2263 (1.50)
Application of 2-year cap	-9.4505*** (2.06)	-2.9961*** (0.55)
Application of 5-year cap	-2.9621 (1.61)	-1.3181*** (0.34)
Number of days restored	0.0075*** (0.00)	-0.0002 (0.00)
Therapeutic categories	Antipsychotics -9.3821* (4.59)	BloodGlucoseRegulators -1.67* (0.84) OphthalmicAgents -1.8760** (0.83) Analgesics -2.4764** (1.03) GeneticCorenzmeDisorderAgents -2.668* (1.00)

Notes:

- Estimated coefficients are given with standard errors in parentheses underneath. Variables are identified as having explanatory power as follows: * $p < .05$, ** $p < .01$, *** $p < .001$. Regression 8 was run with the full dataset of 642 observations, but 13 observations were dropped due to their ability to perfectly predict either success or failure.
- Again, linear regression attempts to model the relationship between two variables by fitting a linear equation to observed data. This study utilizes a multivariate ordinary least squares (OLS) regression, a statistical method of analysis, in order to estimate the relationship between a dependent variable and a collection of independent variables. Specifically, the regressions used in this analysis were:
 - Regression 7: In this OLS regression the dependent variable is the Percent of 14 Years Achieved. The independent variables are listed in the second column of Table 2.
 - Regression 8: This is a probit regression. Statistically, a probit model is a type of regression in which the dependent variable can take only two values. In this case, the dependent variable is Whether the Final Effective Patent Life Was ≥ 12.6 years, and the dependent variable is either “1” (yes, the final effective patent life was ≥ 12.6 years) or “0” (no, the final effective patent life was not ≥ 12.6 years). In this probit regression the dependent variable is a binary indicator of the Percent of 14 Years Achieved. The dependent variables are listed in the second column of Table 2. In the case of 13 observations, they either perfectly predicted success or failure and were therefore dropped.

Table 3
Average Effective Patent Life by Therapeutic Category
Sorted by Average Effective Patent Life with Restoration

Therapeutic Category (n)	Average Length of Clinical Program in Years (Median) (Range)	Average Effective Patent Life Without Restoration in Years (Median) (Range)	Average Effective Patent Life With Restoration in Years (Median) (Range)
Antipsychotics (8)	8.67 (7.96) (2.80, 16.34)	4.51 (3.28) (0.24, 12.14)	8.29 (7.61) (4.21, 14.01)
Sleep disorder agents (6)	4.87 (4.41) (3.42, 6.89)	6.26 (7.00) (-0.79, 11.63)	9.61 (9.04) (2.90, 14.01)
Analgesics (13)	6.76 (7) (2.61, 11.06)	6.75 (7.01) (3.08, 10.36)	9.81 (10.98) (5.08, 13.72)
Antidepressants (16)	8.67 (8.05) (1.74, 16.13)	6.95 (6.88) (-1.50, 13.96)	10.01 (10.52) (2.00, 14.01)
Vaccines (15)	5.56 (5.17) (1.19, 11.70)	6.73 (7.89) (0.02, 12.35)	10.33 (11.36) (2.02, 14.01)
Hormonal (32)	6.51 (6.87) (1.34, 14.32)	7.39 (7.53) (0.02, 13.55)	10.44 (11.56) (2.95, 14.01)
Anticonvulsants (13)	8.11 (7.81) (4.52, 15.07)	6.56 (6.76) (1.34, 13.19)	10.58 (11.76) (6.05, 14.01)
Ophthalmic agents (30)	4.45 (4.27) (1.04, 9.54)	8.17 (8.41) (0.67, 12.98)	10.69 (11.35) (2.67, 14.01)
Respiratory/pulmonary (33)	6.36 (4.95) (1.54, 17.80)	7.62 (8.32) (-2.30, 13.05)	10.84 (12.04) (2.70, 14.01)
Genetic/enzyme disorder agents (7)	5.13 (4.78) (2.21, 11.20)	8.55 (10.04) (2.02, 12.25)	11.03 (12.36) (5.49, 13.18)

Table 3
Average Effective Patent Life by Therapeutic Category
Sorted by Average Effective Patent Life with Restoration

Therapeutic Category (n)	Average Length of Clinical Program in Years (Median) (Range)	Average Effective Patent Life Without Restoration in Years (Median) (Range)	Average Effective Patent Life With Restoration in Years (Median) (Range)
Cardiovascular drugs (192)	5.98 (5.12) (1.88, 15.63)	8.40 (9.26) (-2.70, 13.80)	11.11 (12.63) (2.00, 14.01)
Metabolic bone disease agents (10)	6.72 (6.39) (1.71, 15.37)	7.97 (7.83) (1.61, 12.78)	11.31 (11.58) (4.71, 14.01)
Gastrointestinal drugs (19)	6.55 (5.52) (1.33, 16.92)	8.48 (9.56) (2.31, 13.21)	11.41 (13.40) (6.02, 14.01)
Hematologic agents (35)	5.87 (5.93) (1.60, 13.07)	8.78 (9.73) (1.76, 13.67)	11.73 (13.42) (3.77, 14.01)
Antibacterials (48)	4.61 (4.41) (1.35, 17.25)	9.11 (10.12) (-0.76, 13.86)	11.79 (13.02) (3.69, 14.01)
Antidementia (5)	6.08 (5.21) (2.98, 12.87)	8.67 (7.32) (4.88, 13.07)	11.93 (12.32) (7.80, 14.01)
Antifungals (16)	5.23 (5.21) (1.75, 9.27)	9.43 (10.50) (2.64, 12.52)	12.16 (13.36) (6.18, 14.01)
Antineoplastics (73)	6.47 (6.21) (1.93, 13.31)	9.51 (10.55) (-0.33, 13.80)	12.23 (13.26) (3.36, 14.01)
Blood glucose regulators (23)	5.94 (5.39) (2.45, 12.45)	9.15 (9.27) (3.40, 13.84)	12.29 (12.42) (8.40, 14.01)
Antiemetics (6)	7.17 (7.16) (3.76, 10.44)	8.98 (9.31) (6.11, 12.96)	12.35 (11.90) (11.11, 14.01)

Table 3 Average Effective Patent Life by Therapeutic Category Sorted by Average Effective Patent Life with Restoration			
Therapeutic Category (n)	Average Length of Clinical Program in Years (Median) (Range)	Average Effective Patent Life Without Restoration in Years (Median) (Range)	Average Effective Patent Life With Restoration in Years (Median) (Range)
Genitourinary (13)	5.09 (4.27) (2.47, 9.26)	9.57 (11.11) (2.96, 13.82)	12.46 (14.01) (7.61, 14.01)
Immunological agents (22)	7.12 (6.52) (2.83, 12.96)	9.61 (10.55) (2.89, 13.35)	12.47 (13.90) (6.61, 14.01)
Anesthetics (8)	5.32 (5.32) (2.68, 8.45)	10.37 (11.39) (4.56, 13.67)	12.53 (14.01) (7.09, 14.01)
Antiparkinson (7)	7.22 (7.06) (5.52, 9.68)	9.55 (9.45) (5.22, 12.87)	12.53 (13.74) (10.22, 14.01)
Central nervous system agents (10)	10.64 (8.30) (4.00, 26.22)	9.14 (9.69) (3.41, 12.82)	12.58 (13.78) (8.42, 14.01)
Diagnostic agents (33)	6.19 (5.02) (3.22, 11.36)	10.60 (11.18) (6.00, 13.21)	13.06 (13.72) (11.01, 14.01)
Dermatological agents (17)	5.70 (6.47) (1.18, 9.43)	10.38 (10.84) (4.10, 13.67)	13.16 (14.01) (8.72, 14.01)
Antivirals (29)	4.81 (4.84) (1.84, 10.55)	11.28 (11.92) (5.56, 13.81)	13.18 (14.01) (8.15, 14.01)
Antimigraine (6)	2.99 (2.94) (1.42, 4.75)	11.91 (11.73) (10.51, 13.59)	13.74 (14.01) (12.41, 14.01)

Note: This table includes only therapeutic categories with five or more observations.

Table 4 Determinants of Actual Market Exclusivity			
	Regression 9	Regression 10	Regression 11
Dependent variable	Actual market exclusivity in subset of drugs with generic launch data	Actual market exclusivity in subset of drugs with generic launch data and 17-year patent terms	Actual market exclusivity in subset of drugs with generic launch data and 20-year patent terms
Observations	227	131	96
Adjusted R ²	0.22	0.36 No variables have any explanatory power	-0.26 The regression has no explanatory power
Child patent	Omitted	Omitted	Omitted
Child patent with Transition 17-year term	0.3431 (1.74)	0.8331 (1.90)	Omitted
Child patent with Transition 20-year term	0.3059 (1.66)	Omitted	-2.8069 (1.63)
Child patent with post-URAA 20-year term	-0.2622 (4.05)	Omitted	Omitted
Length of clinical period	-0.0002 (0.00)	-0.0004 (0.00)	0.0031 (0.00)
Length of proxy-preclinical period	-0.0001 (0.00)	-0.0003 (0.00)	0.0040 (0.00)
Transitional 17-year term	1.7915 (1.80)	0.8648 (2.19)	Omitted
Transitional 20-year term	0.2950 (1.49)	Omitted	3.0770 (7.31)
Post-URAA 20-year term	Omitted	Omitted	Omitted
Application of 2-year cap	1.5854 (0.97)	-0.6828 (1.40)	3.2491 (2.45)
Application of 5-year cap	-1.0311 (1.11)	0.3592 (1.48)	-0.2027 (2.15)
Effective patent life after restoration	0.4437* (0.19)	0.4246 (0.22)	2.0309 (1.40)
Number of days restored	0.0018* (0.00)	0.0020 (0.00)	-0.0030 (0.00)
Therapeutic categories			

Notes:

- Estimated coefficients are given with standard errors in parentheses underneath. Variables are identified as having explanatory power as follows: * $p < .05$, ** $p < .01$, *** $p < .001$. Please note that the adjusted R^2 in Regression 11 likely results from a sample size that is too small and independent variables that are correlated.
- Again, linear regression attempts to model the relationship between two variables by fitting a linear equation to observed data. This study utilizes a multivariate ordinary least squares (OLS) regression, a statistical method of analysis, in order to estimate the relationship between a dependent variable and a collection of independent variables. The regression used in this analysis was:
 - Regression 9: In this OLS regression the dependent variable is the actual market exclusivity in the subset of drugs with generic launch data. The coefficients of the independent variables are listed in the second column of Table 4.
 - Regression 10: In this OLS regression the dependent variable is actual market exclusivity in subset of drugs with generic launch data and 17-year patent terms. The coefficients of the independent variables are listed in the third column of Table 4. None of the independent variables have any explanatory power.
 - Regression 11: In this OLS regression the dependent variable is the actual market exclusivity in subset of drugs with generic launch data and 20-year patent terms. The coefficients of the independent variables are listed in the fourth column of Table 4. The regression has no explanatory power.