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Mr. Chairman and esteemed members of the Committee, it is an honor to testify before you today. To supplement my oral testimony, I am submitting the following written materials excerpted from academic work recently published in the Harvard Journal on Legislation. These excerpts chronicle a new generation of anticompetitive strategies that are used to block the entry of generic drugs. The work is titled, "Drug Wars: A New Generation of Generic Pharmaceutical Delay," and the full article is available at http://papers.ssrn.com/sol3/papers.cfm?abstract_id=2659308.

DRUG WARS: A NEW GENERATION OF GENERIC PHARMACEUTICAL DELAY

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Thirty years ago, Congress ushered in a new and miraculous era in medicine with the creation of the Hatch-Waxman system for approval of generic drugs. The progress, however, has not been without resistance. This Article presents an overview of three generations of games pharmaceutical companies play to keep generics off the market and maintain monopoly pricing….Generation 3.0 uses administrative processes, regulatory schemes, and drug modifications to prevent generics from getting to market. Some of these schemes have now made the news as debates rage over pharmaceutical pricing.

Society, however, cannot necessarily blame companies for engaging in behavior that is strongly in their economic self-interest. One cannot expect mice to run in the appropriate direction if the cheese is located at the other end. Thus, this Article's goals are two-fold: first, to shine light on the complex behaviors as they are unfolding, and second, to explore the contours of how new approaches could be structured. To paraphrase one former FDA commissioner, we do not want the most creative activity at pharmaceutical companies to take place in the legal department. And after thirty years of experience with Hatch-Waxman, it is time for the next phase.

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I. INTRODUCTION

In most pharmaceutical transactions, patients seamlessly realize the benefits of generic drugs. A doctor's written prescription for Pfizer's Zoloft is substituted for a generic bottle of sertraline by the time the patient reaches the pharmacy. Patients who present with standard sinus infections will probably leave their neighborhood drug store with the classic five-day boxes of azithromycin for $10,[1] rather than boxes actually branded as a Zithromax Z-Pak. Automatic substitution is led by the pharmacist, who is generally permitted to substitute a generic for a branded drug when available, and the public enjoys billions of dollars of savings with no action required on the part of either patients or doctors.[2] The patient's incentives are also usually aligned with those of insurers and other payors, who wish to pay less when- ever possible and thus heavily promote the use of generics.

Today, 88% of all prescriptions in the U.S. are filled using generic medication,[3] and 81% of all small-molecule drugs have a generic equivalent.[4] When a generic is introduced into a market previously monopolized by a brand-name drug, the generic drug normally enters at a 20% discount from

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[1] *See* IMS INST. FOR HEALTHCARE INFORMATICS, MEDICINE USE AND SHIFTING COSTS OF HEALTHCARE: A REVIEW OF THE USE OF MEDICINES IN THE UNITED STATES IN 2013, at 15 (Apr. 2014), http://www.imshealth.com/en/thought-leadership/ims-institute/reports/use-of-medicines-in-the-us-2013#ims-form [https://perma.cc/2QX9-AS8V] ("The average co-pay for 78.6% of all retail dispensed prescriptions was $10 or less.").

[2] *See* Michael A. Carrier, *A Real-World Analysis of Pharmaceutical Settlements: The Missing Dimension of Product Hopping*, 62 FLA. L. REV. 1009, 1017 (2010). Automatic substitution laws, known as state drug product selection ("DPS") laws, exist in all fifty states. In some states, automatic substitution is required when the generic equivalent is available.

[3] *See Implementation of the Generic Drug User Fee Amendments of 2012 (GDUFA): Hearing Before the H. Comm. on Oversight & Gov't Reform*, 114th Cong. 1 & chart.1 (2016) (statement of Janet Woodcock, Director, Ctr. for Drug Evaluation & Res., U.S. Food & Drug Admin.); *see also* IMS INST. FOR HEALTHCARE INFORMATICS, *supra* note 1, at 51.

[4] *See* Ernst R. Berndt & Murray L. Aitken, *Brand Loyalty, Generic Entry and Price Competition in Pharmaceuticals in the Quarter Century After the 1984 Waxman-Hatch Legislation* 4, 6 (Nat'l Bureau of Econ. Research, Working Paper No. 16431, 2010), http://www.nber.org/papers/w16431.pdf [http://perma.cc/7YPB-KQBF].

the branded medication within six months of launch, and the price falls quickly from that point.[5] Eventually, most generics are priced at an 80% to 85% discount from their name-brand equivalents.[6] Prices can even fall to 10% of the original cost when many generics enter the market.[7] Within a year of generic introduction, the name-brand drug generally loses an average of 80% to 90% of its market share.[8] The FDA estimates that consumers saved over $217 billion in 2012 alone through the use of generics,[9] with total savings of $1.68 trillion from 2005 to 2014.[10]

The introduction of generic competitors is tough on a brand-name drug company, which must face the loss of its monopoly status and the resulting severe drop in price. Nevertheless, the design of the patent system dictates that a patent holder's right to exclude others from the market must end with the expiration of the patent.

One might call the generic revolution a miracle, but it certainly did not occur naturally or serendipitously. The underlying mechanism behind it is particularly complex. Generic drug entry is covered by the Drug Price Competition and Patent Term Restoration Act, commonly known as the Hatch-Waxman Act.[11] Passed in 1984, Hatch-Waxman created a pathway to generic entry meant to incentivize the speedy introduction of generic drugs to market. Before the Act, generic entry into the market was slow.[12] Would-be generic manufacturers could not apply to enter the market until after the branded company's patents had expired, with the effect that brand-name companies enjoyed a de facto patent extension and ongoing monopoly profits as the generic awaited FDA approval.[13] Further, few generics were entering the market to begin with. The burden of the application process (which

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[5] *See id.* at 9–10, 10 fig.2.

[6] *See Facts About Generic Drugs*, U.S. FOOD & DRUG ADMIN., http://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingGenericDrugs/ucm167991.htm [http://perma.cc/GQ92-QEN4] (last updated June 19, 2015).

[7] *See* Berndt & Aitken, *supra* note 4, at 9, 10 fig.2.

[8] *See id.*; *see also* Henry G. Grabowski et al., *Evolving Brand-Name and Generic Drug Competition May Warrant a Revision of the Hatch-Waxman Act*, 30 HEALTH AFF. 2157, 2163 exhibit 4 (2011). In fact, for the period between 2004 and 2008, Grabowski *et al.* found that the average drug with more than $1 billion in annual sales had more than ten generic competi- tors one year after first generic entry. *See id.* at 2160 exhibit 1.

[9] GENERIC PHARM. ASS'N, GENERIC DRUG SAVINGS IN THE U.S. 1 (2013), http://www.gphaonline.org/media/cms/2013_Savings_Study_12.19.2013_FINAL.pdf [http://perma.cc/2EW2-6W6F] (data supplied by IMS Health).

[10] *Implementation of the Generic Drug User Fee Amendments of 2012 (GDUFA): Hearing Before the H. Comm. on Oversight & Gov't Reform*, 114th Cong. 1 (2016) (statement of Janet Woodcock, Director, Ctr. for Drug Evaluation & Res., U.S. Food & Drug Admin.).

[11] Drug Price Competition and Patent Term Restoration Act, Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified as amended in scattered sections of 21 U.S.C. and 35 U.S.C.).

[12] *See* WENDY H. SCHACHT & JOHN R. THOMAS, CONG. RES. SERV., REPORT R41114, THE HATCH-WAXMAN ACT: A QUARTER CENTURY LATER, at Summary (2011), http://congressional.proquest.com/profiles/gis/result/pqpresultpage.gispdfhitspanel.pdflink/$2fapp-bin$2fgis-congresearch$2ff$2fa$2f7$2f8$2fcrs-2011-rsi-0151_from_1_to_20.pdf/entitlementkeys=1234%7Capp-gis%7Ccongresearch%7Ccrs-2011-rsi-0151 [http://perma.cc/M2MP-F7KQ].

[13] ROBIN FELDMAN, RETHINKING PATENT LAW 159 (2012).

required the generic to complete its own clinical trials) and the lack of substantial profits deterred most manufacturers.[14]

As discussed in more detail in Part II, Hatch-Waxman offers generics a number of incentives to enter the market as quickly as possible. First, pharmaceutical firms can submit an abbreviated new drug application ("ANDA") before the patents for the brand-name drug have expired.[15] ANDAs only need to contain evidence that the generic is bioequivalent and has the same pharmacokinetic profile as the brand-name drug; they can rely on the brand-name drug company's clinical trial data to meet the rest of the application requirements, including those related to the safety and efficacy of the drug.[16] Second, in what is known as a Paragraph IV certification, a generic manufacturer can attempt to enter the market before the pioneer's patent term(s) have expired, generally triggering litigation from the branded firm.[17] As a reward for facing the costs and risks of litigation, the first generic manufacturer to file a Paragraph IV ANDA and gain approval generally is entitled to 180 days of market exclusivity alongside the brand-name drug.[18] In other words, during the 180-day period, only the brand-name drug and the first generic filer are allowed to be on the market. While only six months long, this duopoly period can be extremely valuable, worth hundreds of millions of dollars for blockbuster drugs.[19] This benefit is intended to give generic companies an incentive to challenge weak patents or patents that should not cover the drug at issue.

The Hatch-Waxman Act has overwhelmingly met Congress' goals of balancing adequate patent protection for pioneer inventors with promoting the rapid introduction of generics once this patent protection has expired. Since 1984, more than 10,000 generics have entered the market,[20] and the percentage of prescriptions filled with generics has risen from just 13% in 1980[21] to around 86% by 2013.[22] Most important, generic manufacturers have the incentive and ability to enter the market immediately after (or even before) the original patent terms expire.

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[14] *See* Elizabeth S. Weiswasser & Scott D. Danzis, *The Hatch-Waxman Act: History, Structure, and Legacy*, 71 ANTITRUST L.J. 585, 585–90 (2003) (discussing the absence of generics on the market before the adoption of Hatch-Waxman).

[15] 21 U.S.C. § 355(j) (2012).

[16] 21 U.S.C. §§ 355(j)(2)(A)(i)–(v) (2012).

[17] 21 U.S.C. § 355(j)(2)(A)(vii)(IV) (2012).

[18] 21 U.S.C. § 355(j)(5)(B)(iv) (2012). Exceptions and stipulations will be discussed in Part II.

[19] *See* Matthew Avery, *Continuing Abuse of the Hatch-Waxman Act by Pharmaceutical Patent Holders and the Failure of the 2003 Amendments*, 60 HASTINGS L.J. 171, 178 & 178 nn.55–56 (2008).

[20] *See* SCHACHT & THOMAS, *supra* note 12, at 5; *see also Medicare Prescription Drug, Improvement, and Modernization Act: Hearing on H.R. 1 Before S. Comm. on the Judiciary*, 108th Cong. (2003) (statement of Daniel E. Troy, Chief Counsel, U.S. Food & Drug Admin.), http://www.fda.gov/newsevents/testimony/ucm115033.htm [https://perma.cc/3TP7-BEZY].

[21] CONG. BUDGET OFFICE, HOW INCREASED COMPETITION FROM GENERIC DRUGS HAS AFFECTED PRICES AND RETURNS IN THE PHARMACEUTICAL INDUSTRY 37 (1998).

[22] IMS INST. FOR HEALTHCARE INFORMATICS, *supra* note 1, at 51.

The actual miracle, however, is not the dramatic rise of generics. Rather, the miracle is that the benefits of Hatch-Waxman have largely held up despite its complexity and the persistent attempts at undercutting its aims. Hatch-Waxman has created a veritable playground of opportunities that pharmaceutical companies have used to hold off generic competition. This is understandable. The temptation to avoid the impact of Hatch-Waxman can be overpowering when even a few months of additional monopoly profits can be worth hundreds of millions of dollars or more.[23] This encourages companies to expend tremendous energy blocking generic entry by any means possible, with some companies using ever more clever and complicated strategies. As a result, many pharmaceutical firms may no longer compete solely on the basis of innovation, but rather on their ability to manipulate policy mechanisms and pathways to extend monopoly and duopoly terms.

This behavior undermines the goals of the patent system and can provide less than optimal innovation effects. One cannot fully blame companies, however, for engaging in behavior that is strongly in their economic self-interests. If society wishes its interests to prevail, then the legal system must bring the incentives of the players into proper alignment with the goals of society—either by creating sufficient incentives or sufficient disincentives. One cannot expect the rats in the maze to run in the direction society wishes if the cheese is located at the other end. And, as the system currently operates, the cheese is poorly located.

The goal of this paper is two-fold: first, to shine light on complex behaviors as they are unfolding and, second, to suggest ways to cabin those behaviors and create incentives for companies to follow the path that is optimal for society. Pharmaceutical companies should be directing their creative energies toward research and development, not toward inventing new legal challenges and regulatory obstructions.

To be clear, when pharmaceutical companies preserve their hard-earned patent exclusivity by legally knocking down generic challenges, such behavior is consistent with societal goals and important for the patent system. Rights are worth little if the rights-holder cannot enforce them, and that is as true for patents as for any form of legal right. In contrast, when firms attempt to unlawfully extend their monopolies, such behavior undercuts the goals of the patent system, and the cost to society can be troubling. Patients and the general public lose, giving up billions of dollars in savings while

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[23] For example, Gilead's Hepatitis C drug, Sovaldi, earned $7.9 billion in sales in 2014, making it the top-earning drug in the United States. Three additional months of sales at that rate would be worth $1.98 billion. Pfizer's Nexium took in $5.9 billion in revenue in the same year—three additional months would be worth $1.48 billion. Lacie Glover, *Here Are the Top- Selling Drugs in the US*, TIME (June 26, 2015), http://time.com/money/3938166/top-selling- drugs-sovaldi-abilify-humira/?xid=soc_socialflow_twitter_money [http://perma.cc/5K4R- SLM2]. Fifty-five drugs earned more than $1 billion in revenue in 2013. *U.S. Pharmaceutical Sales—2013*, DRUGS, http://www.drugs.com/stats/top100/2013/sales [https://perma.cc/3Q4Z- TVZT] (last updated Feb. 2014).

ready-to-market generics languish on the sidelines. The energy spent on manipulation of the legal system diverts time and resources away from innovation activities.

This Article presents a broad overview of the "games" pharmaceutical companies play to keep valuable generics away from consumers while enriching their own profits. [New] approaches focus on the active obstruction of generic entry by branded firms, somewhat like tripping other kids on their way to the playground. These new, combative strategies make up the focus of this Article.

This Article proceeds in five Parts. Part II explains the Hatch-Waxman Act pathway to generic entry in more detail, discussing the economic forces of the pharmaceutical market and amendments designed to improve the functioning of the Act. Part III discusses the origins of generic delay tactics, called "Generation 1.0"—the first of three "generations" the Article uses to categorize the tactics that have evolved over time. The organizational system of generations is not meant to suggest that these each of these periods has taken place sequentially and separately. Some "Generation 1.0"-style settlements still survive; early "Generation 3.0" tactics have plagued generics for more than a decade—the overlap between generations can be substantial. Instead, the system serves as a helpful way of organizing sets of related tactics, and the use of "generations" implies that each era of tactics has evolved from or developed in response to strategies from previous generations. . . .

Part V provides a comprehensive look at emerging "Generation 3.0" strategies—tactics that, so far, have been deployed largely under the radar. By detailing this new generation of difficult-to-detect behaviors, the hope is that policymakers and academics can develop appropriate responses to the entire panoply of Hatch-Waxman manipulation. Generation 3.0 tactics no longer focus on delay agreements with generic competitors, but rather on using administrative processes, regulatory schemes with connections to Hatch-Waxman, and drug modifications to obstruct generics from getting to market. Many of these strategies have little justification beyond obstruction of generics, and some recent fact patterns are falling further outside the boundaries of common sense. Specifically, Part V will discuss delay mechanisms including labeling changes, using FDA safety restrictions as an excuse for delay, and sham litigation, as well as "multiplicity tactics," in which a number of these mechanisms are exploited at once. Some of these strategies have been part of recent schemes to restrict generic substitution while simultaneously raising prices of the brand-name drug, leading to a swell of public outrage in fall 2015 and the return of pharmaceuticals as a key policy topic.

Part VI concludes with ideas for reforming the generic entry pathway. These ideas borrow from systems theory—looking from the perspective of how different systems interact to create opportunities and incentives to correct suboptimal behaviors. Moreover, to move the system away from hide-

and-seek games, this section proposes the addition of standards-based legal rules. Most important, to avoid "death by tinkering"[24]—that is, adjusting doctrines a little here and a little there without comprehensive logic until the entire area collapses under its own weight—this section suggests a deeper

look and a more comprehensive overhaul of different intersecting regimes. Hatch-Waxman was indeed a brilliant legislative innovation, heralding nothing short of a miracle in the reduction of drug costs. Now, it is time to consider the next generation of the regime so those miracles are not swept away.[25]

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[24] *See* Robin Feldman, *A Conversation on Judicial Decision-Making*, 5 HASTINGS SCI. & TECH. L.J. 1, 2 (2013) (introducing the phrase "death by tinkering" to describe patent jurispru- dence in the Federal Circuit).

[25] *See generally* Aaron S. Kesselheim & Jonathan J. Darrow, *Hatch-Waxman Turns 30: Do We Need a Re-Designed Approach for the Modern Era?*, 15 YALE J. HEALTH POL'Y L. &

II. THE WINDING ROAD TO GENERIC ENTRY

The Hatch-Waxman Act is a deeply complex piece of legislation, codified in four different sections of the United States Code.[26] While it creates a streamlined pathway for generic manufacturers to seek approval of their drug, it does so in a way that testifies to the difficulty of satisfying all stake-holders in the pharmaceutical market. The goal of protecting innovative activity, balanced with the desire to make low-cost drugs available to patients, has produced a labyrinthine series of statutes. Complexity breeds opportunity, however, and Hatch-Waxman's legacy is littered with evidence of manipulation.[27]

This Part focuses on the core components of Hatch-Waxman most often implicated in generic delay, in the clearest terms possible, omitting discussions of exceptions and complex subsections where appropriate. Later Parts of this Article will introduce other sections of the Act when needed to help make sense of these intricate games of generic delay, including descriptions of amendments meant to tighten the functioning of Hatch-Waxman (while frequently creating their own difficulties).

Hatch-Waxman created a new framework for the approval and marketing of generic medications. Prospective generic manufacturers can submit an Abbreviated New Drug Application, almost exclusively referred to as an "ANDA," to seek approval of a drug equivalent to a reference drug already approved by the FDA.[28] The ANDA must be for a medication bioequivalent to the brand-name drug,[29] and it must generally have the same active ingredient, route of administration, dosage form, strength, use indications, and labeling information as the existing medication.[30] An ANDA, however, can make use of a branded drug company's pre-existing clinical trial data that proves the safety and efficacy of the drug.[31] This saves the applicant the years of work and great expense necessary to conduct new clinical trials.

The Hatch-Waxman Act expressly allows the activity necessary to produce an ANDA to take place without triggering an act of patent infringement. The use of the patent holder's data and trial information, as well as samples of the actual drug to test for bioequivalence, are all exempt from an assertion of patent infringement when used for ANDA development.[32] The

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ETHICS 293 (2015) (presenting another recent article reviewing the history of Hatch-Waxman and suggesting improvements).

[26] Drug Price Competition and Patent Term Restoration Act, Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified as amended in scattered sections of 21 U.S.C. and 35 U.S.C.).

[27] FELDMAN, *supra* note 13, at 160 ("As so often is the case, complexity breeds opportunity, and clever lawyers have been exploiting the details of the act since its inception.").

[28] 21 U.S.C. § 355(j) (2012).

[29] The Act defines two drugs as bioequivalent when "the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug." 21 U.S.C. § 355(j)(8)(B) (2012).

[30] 21 U.S.C. § 355(j)(2)(A) (2012).

[31] *See* SCHACHT & THOMAS, *supra* note 12, at 1.

[32] 35 U.S.C. § 271(e)(1) (2012).

exemption allows generics to be ready for entry by the moment of patent expiration at the latest, rather than having to wait for patent expiration and only then begin the process for approval. Prior to Hatch-Waxman, brand-name drug companies enjoyed a lengthened patent term because no generic could be ready to market when the patent expired.[33]

When the brand-name drug company originally files for FDA approval, the law requires that the company list all patents that "could reasonably be asserted" against a generic applicant.[34] These are then recorded in an FDA document commonly referred to as the "Orange Book."[35] The Orange Book has played a prominent role in some of the game playing that has unfolded across time, as described below.

When a generic drug maker files an ANDA, it must make one of four "certifications" to each of the patents the brand-name drug maker has listed for the medication in the Orange Book.[36] Most of these certifications result in limited fuss and bother because they either represent that all the patents have expired, that no patents are listed in the Orange Book, or that the generic company will wait until all patents expire before bringing the drug to market.[37]

All the action, however, is in what is known as a "Paragraph IV certification." A Paragraph IV certification alleges that the listed patent is either invalid or would not be infringed by the generic drug.[38] In essence, this represents an attempt by the generic to enter the market before expiration of a listed Orange Book patent, and it is the core mechanism of Hatch-Waxman. The entire Paragraph IV process is intended to encourage generic companies to challenge weak patents as well as to give generics the incentive to do battle with big pharmaceutical companies.

A Paragraph IV certification is treated as an "artificial" act of patent infringement. This allows the brand-name drug company to initiate litigation, which it must do within forty-five days of receiving notification from the ANDA filer. Otherwise, the FDA may approve the application.[39]

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[33] *See* Roche Prods., Inc. v. Bolar Pharm. Co., 733 F.2d 858, 863–64 (Fed. Cir. 1984) ("The [brand-name companies] gain for themselves, it is asserted, a *de facto* monopoly of upwards of 2 years by enjoining FDA-required testing of a generic drug until the patent on the drug's active ingredient expires."). The case found that use of a patent-protected drug for the tests necessary for generic development was a prohibited use. Hatch-Waxman was signed into law five months later.

[34] 21 U.S.C. § 355(b)(1) (2012).

[35] FELDMAN, *supra* note 13, at 160–61. The formal name of the Orange Book is the "Approved Drug Products with Therapeutic Equivalence Evaluations." *See Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations*, U.S. FOOD & DRUG ADMIN. (May 17, 2013), http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm [https://perma.cc/WY66-RYJZ].

[36] *See* 21 U.S.C. § 355(j)(2)(A)(vii) (2012); *see also* 21 U.S.C. § 355(j)(7)(A) (2012) (describing the workings of the Orange Book).

[37] *See* 21 U.S.C. §§ 355(j)(2)(A)(vii)(I)–(III) (2012).

[38] 21 U.S.C. § 355(j)(2)(A)(vii)(IV) (2012).

[39] *See* 21 U.S.C. § 355(j)(5)(B)(iii) (2012).

Why would a generic applicant purposely choose to bring on costly and potentially damaging litigation? First, there are certainly weak patent claims, and generic companies have enjoyed considerable success challenging drug patents.[40] Second, baked into Hatch-Waxman is a significant incentive for the first filer submitting a generic application with a Paragraph IV certification to at least one of the listed patents for the drug: as long as the first filer does not lose its patent infringement case, it is generally entitled to 180 days of marketing exclusivity alongside the brand-name drug.[41] In other words, for about six months, only the brand-name drug company and the first generic can sell the drug; no other generic company can come to market. This essentially creates a duopoly between the brand and generic for the first 180 days after the generic enters, which normally occurs after one of the following events: all relevant patents and exclusivities expire; the generic drug maker wins a challenge invalidating all relevant patents or finding that infringement did not occur; or the generic company reaches a settlement with the branded drug maker allowing entry.[42] This exclusivity period can easily be worth hundreds of millions of dollars to a generic, representing a substantial majority of the potential profits to be gained from generic entry.[43]

The Paragraph IV first-filer exclusivity is thus an enormous incentive for a generic applicant to file as soon as possible and secure the 180 days of exclusivity, as well as potential market entry long before drug patent expiration. The artificial nature of the patent infringement action is also helpful. It allows the generic to trigger litigation without actually entering the market and potentially accruing substantial damages. This complicated and lucrative pathway also has made Hatch-Waxman susceptible to abuse, mainly because of the economic incentives created by the exclusivity period.[44]

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[40] *See* FED. TRADE COMM'N, GENERIC DRUG ENTRY PRIOR TO PATENT EXPIRATION 16 (2002), https://www.ftc.gov/sites/default/files/documents/reports/generic-drug-entry-prior-patent-expiration-ftc-study/genericdrugstudy_0.pdf [http://perma.cc/H8FY-J3AC] (finding that ANDA filers won their Paragraph IV challenge 73% of the time).

[41] *See* 21 U.S.C. § 355(j)(5)(B)(iv) (2012). After 2003 amendments to Hatch-Waxman, it is possible to forfeit the 180-day exclusivity period without losing a patent infringement case. *See infra* Part III. Further, it is also possible that the brand-name drug company chooses not to bring litigation during the forty-five day period. In this case, the first-filer still retains its rights to 180 days of exclusivity.

[42] During the 180-day period, the FDA is not permitted to approve any other generic applications that have a Paragraph IV certification. *See* 21 U.S.C. §§ 355(j)(5)(B)(iv)(I)–(II) (2012). However, this does not entirely prevent the presence of other competition. Brand-name companies can launch their own generic version of the drug at a lower price tier (or permit another company to do so), creating instant competition for the generic. These generics are often called "authorized generics," and are discussed infra in Part IV.

[43] *See* Avery, *supra* note 19, at 178, 178 nn.55–56.

[44] When there are multiple first-filing ANDA applicants (all submitting on the same day, usually the first day that ANDAs will be accepted), all applicants are eligible for exclusivity. *See generally* U.S. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY 180-DAY EXCLUSIVITY WHEN MULTIPLE ANDAS ARE SUBMITTED ON THE SAME DAY (2003), http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm072851.pdf [https://perma.cc/PAE4-6LWE].

If the patent holder chooses to initiate litigation, a thirty-month stay is placed on generic approval, with the goal of allowing the infringement litigation to work through the courts while the FDA is reviewing the generic application.[45] The generic application cannot be approved during the following thirty months, unless a court enters a final order declaring the patents at issue invalid, unenforceable, or not infringed.[46]

Although Hatch-Waxman generally is discussed in the framework of generic drugs, the Act also was designed to add new protections for brand-name drug companies. Between the Patent and Trademark Office's ("PTO") patent approval process and the FDA's own approval process for the drug (which generally overlaps with a portion of the patent term), the effective life of a drug patent is often substantially shorter than the twenty-year term of most patents.[47] Thus, Hatch-Waxman allows pharmaceutical companies to receive an extension of the patent term to partially "restore" the time lost to approval processes.[48] This "restoration" is the origin of the Hatch-Waxman Act's full name, the Drug Price Competition and Patent Term *Restoration* Act.

The Act also provides certain new drugs with specified non-patent exclusivities. For example, drugs with a new active ingredient never before approved by the FDA are eligible for five years of marketing exclusivity, in what is known as new chemical entity ("NCE") exclusivity.[49] This is not an extension of the patent term—it only means that the FDA is not allowed to accept applications for generic versions of the drug for at least four years after initial FDA approval. This, however, gives the brand-name drug maker breathing space before a generic company can start the ball rolling. Similar exclusivities are available for new clinical studies that lead to new drug indications or formulations (three years) and, as established by the Orphan Drug Act, drugs with indications to treat defined rare diseases (seven years of marketing exclusivity).[50] A six-month exclusivity extension for all approved indications is available when the drug undergoes pediatric studies requested by the FDA.[51]

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[45] *See* 21 U.S.C. § 355(j)(5)(B)(iii) (2012).

[46] *See id.* If the first Paragraph IV generic filer loses its case, it forfeits the 180-day exclusivity period, and the Paragraph IV certification is usually changed to a Paragraph III certification agreeing to not enter until the expiration of all FDA and patent exclusivity. *See Small Business Assistance: 180-Day Generic Drug Exclusivity*, U.S. FOOD & DRUG ADMIN., http://www.fda.gov/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/ucm069964.htm [https://perma.cc/NX69-FPMU] (last updated Feb. 11, 2016).

[47] *See* SCHACHT & THOMAS, *supra* note 12, at 3.

[48] *See* 35 U.S.C. § 156(g)(6)(A) (2012); 35 U.S.C. § 156(c) (2012). *See generally* 35 U.S.C. § 156 (describing the full patent term extension process).

[49] *See* 21 U.S.C. § 355(c)(3)(E)(ii) (2012); 21 U.S.C. § 355(j)(5)(F)(ii) (2012).

[50] *See* 21 U.S.C. § 355(c)(3)(E)(iii) (2012); 21 U.S.C. §§ 355(j)(5)(F)(iii)–(iv) (2012) (explaining new clinical study exclusivity); 21 U.S.C. §§ 360bb–360cc (2012) (explaining Orphan Drug Act definitions and exclusivities).

[51] *See* 21 U.S.C. §§ 355(a)–(c) (2012); *see also* Kurt R. Karst, *Pediatric Exclusivity: Amazingly Powerful, Essentially Ironclad . . . and Often Overlooked*, FDA L. BLOG (July 7, 2015, 7:59 PM), http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2015/07/pediatric-

Important changes have been made to Hatch-Waxman and its related mechanisms since its enactment, most notably through the Medicare Modernization Act in 2003 and the Food and Drug Administration Amendments Act of 2007.[52] With many of the changes aimed at curbing abuses and plugging loopholes in Hatch-Waxman, a number of these modifications will be discussed in future Parts when relevant.

In short, Hatch-Waxman set the stage for a new era in medicines: generic competitors were able to develop and test their products, as well as apply for FDA approval, before the expiration of the brand-name drug company's patent. In addition, the legislation created incentives for generics to challenge weak patent claims. The goal, of course, was to speed generic versions of drugs to market as quickly as possible, introducing competition and dramatically lowering prices for consumers. . . .

III. "GENERATION 3.0" . . . ACTIVE OBSTRUCTION OF GENERICS

A. General Description and the Economics at Play

[B]rand-name drug companies are turning to new strategies that actively obstruct generics from entering the market. The point of obstruction can come at different stages of

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that [these aspects] . . . were outweighed by the anticompetitive harm of the no-AG agreement." *Id.* at 410.

[129] *Id.* at 405.

[130] *Id.* at 406–07, 406 n.27.

[131] *Id.* at 405.

[132] *Id.* at 404 n.21 (citing FED. TRADE COMM'N, *supra* note 119, at iii). The Court used the term "generic duopoly" to describe when the brand-name drug company and the first generic are both in the market with generic versions. It should be noted, however, that this market structure is different from what economists generally refer to as a duopoly, which occurs when the original drug maker is selling its own branded drug and the first generic is selling a generic version. In contrast, the court's "generic duopoly" market may feature three versions of the drug on the market—the brand-name drug and two generic versions—one made by the original drug maker and one made by the first filing generic.

generic development: before an ANDA is submitted, during the ANDA approval process, after a generic drug has been approved for marketing, or even once the generic has managed to enter the market.

As this Part will explain, the mechanisms of obstruction are varied and complex, but most use strategic behavior in the generic substitution system or in FDA regulatory processes to attempt a delay. In cases of what is known as "product hopping," for example, the brand-name drug company takes advantage of its market power to shift pharmacists, doctors, and consumers to new versions of drugs before a generic for the "old" version is able to reach the market.[133] A second mechanism uses FDA guidelines meant to ensure the safe use of potentially dangerous or potent drugs to prevent potential generic manufacturers from accessing drug samples necessary to test for bioequivalence. A third uses a process available to the public to raise concerns about pharmaceuticals in order to bring about a FDA review of the petition during which ANDA approval will be delayed—knowing full well that the FDA is likely to take months (or longer) to review even entirely groundless claims.

The new obstruction strategies may result in anywhere from a few months up to a couple years of delay, in contrast to the multiple years of delay that reverse payment agreements can create.[134] Obstruction strategies also are unlikely to be successful beyond the months of delay garnered by filing an FDA petition or refusing to deal drug samples. Many of the attempts are likely to be rejected by the FDA. Nevertheless, even a rejected or dismissed attempt at obstruction can be worth hundreds of millions of dollars. [D]elay can be extremely valuable—if a branded drug has $1 billion in annual U.S. sales, an agreement with the generic to delay entry for three to four years is worth billions to the brand-name company—even when factoring in the cost of paying of the generic to delay.[135] If those settlements are not available, however, any form of delay is valuable if the costs and risks are low.

Consider the example of a citizen petition asking the FDA to delay approval for a generic.[136] The cost of filing a citizen petition is trivial com-

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[133] *See* HERBERT HOVENKAMP ET AL., IP AND ANTITRUST: AN ANALYSIS OF ANTITRUST PRINCIPLES APPLIED TO INTELLECTUAL PROPERTY LAW § 12.5 (1st ed. 2002) (discussing "product hopping").

[134] There are, of course, exceptions and edge cases where "Generation 3.0" strategies have been successful in achieving several years of generic entry delay. Product hopping, in particular, has been an effective mechanism for longer-term delay.

[135] See Part III for more discussion about the economics behind pay-for-delay. Further, the estimate above of the value of pay-for-delay is not unreasonable. Of the top 100 drugs in the United States by revenue in 2013, the median drug had sales over $1 billion. *U.S. Pharmaceutical Sales-2013*, DRUGS.COM, http://www.drugs.com/stats/top100/2013/sales [https://perma.cc/3Q4Z-TVZT] (last updated Feb. 2014) (reporting sales data for Lovaza and Gilenya, the 50th and 51st best-selling drugs, respectively). If the brand-name manufacturer is able to broker a delay of three years for $500 million, the branded manufacturer gets $2.5 billion out of the deal, assuming that branded sales are negligible after generic introduction.

[136] The details of the citizen petition process will be explained infra at Section V.D.

pared to the expected value of the benefits, even if success is unlikely.[137] Although recent FDA guidance requires that citizen petitions with the potential to affect generic approval must be considered within 150 days,[138] those approximately five months of delay could be worth hundreds of millions of dollars in additional monopoly revenues as the generic sits on the sideline waiting for approval.[139] It is not billions, but it will do. In short, the new strategies might impact a shorter term with lower rewards, but their minimal cost makes them worth a try when some not entirely baseless claim or objection can be produced.[140]

[Take] the example of *In re Flonase Antitrust Litigation*.[141] At its peak, Flonase, a steroid nasal spray for allergy treatment, reached $1.3 billion a year in sales.[142] Through a complicated series of citizen petitions, GlaxoSmithKline was able to stave off generic entry for twenty-three months.[143] Thus, the delay achieved through citizen petitions was worth approximately $2.5 billion, assuming it maintained the peak $1.3 billion in sales per year. In two class action lawsuits that were later filed against Glaxo, the company settled for a total of

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[137] *See* Darren S. Tucker, *FDA Citizen Petition: A New Means of Delaying Generic Entry?*, 20 ANTITRUST HEALTH CARE CHRON. 10, 11 (2006) (citing Comment of the Staff of the Bureau of Competition & the Office of Policy Planning of the Fed. Trade Comm'n Before the Food & Drug Admin. In the Matter of Citizen Petitions; Actions That Can Be Requested by Petition; Denials, Withdrawals, and Referrals for Other Administrative Action, FDA Docket No. 99N-2497, at *4, 6–7 (Mar. 2, 2000), https://www.ftc.gov/sites/default/files/documents/advocacy_documents/ftc-staff-comment-food-and-drug-administration-concerning-citizen-petitions/v000005.pdf [https://perma.cc/AP3K-LVM4]).

[138] U.S. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: CITIZEN PETITIONS AND PETITIONS FOR STAY OF ACTION SUBJECT TO SECTION 505(Q) OF THE FEDERAL FOOD, DRUG AND COSMETIC ACT 3 (Nov. 2014), http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm079353.pdf [https://perma.cc/ZEX4-QLLG] (discussing Section 505(q)(1)(F)).

[139] This calculation assumes the same $1 billion in annual sales for a top 100 drug used in note 135.

[140] Granted, the cost of these strategies could climb much higher than $25,000 as companies begin to face antitrust litigation for their actions and must expend millions on legal fees after the fact. Until these cases are regularly ending in settlements worth billions to the plaintiffs, however, these "games" are still valuable for brand-name drug companies.

[141] *In re* Flonase Antitrust Litig., 951 F. Supp. 2d 739 (E.D. Pa. 2013) (approving direct purchaser settlement); *In re* Flonase Antitrust Litig., 291 F.R.D. 93 (E.D. Pa. 2013) (approving indirect purchaser settlement). Further, the value of this strategy is higher considering the possibility that the petition or request of the brand might actually be accepted. For example, some have found that the FDA granted about twenty percent of the citizen petitions filed by brands against generics between 2008 and 2010. Michael A. Carrier & Daryl Wander, *Citizen Petitions: An Empirical Study*, 34 CARDOZO L. REV. 249, 276 (2012), http://cardozolawreview.com/content/34-1/Carrier.34.1.pdf [https://perma.cc/J8ND-2FGC].

[142] Tracy Staton, *GSK Reaches $150M Deal in Flonase Antitrust Case*, FIERCEPHARMA (Dec. 20, 2012), http://www.fiercepharma.com/story/gsk-reaches-150m-deal-flonase-antitrust-case/2012-12-20 [https://perma.cc/9QZX-QDD3].

[143] *See* Seth C. Silber, Jonathan Lutinski & Rachel Taylon, *Abuse of the FDA Citizen Petition Process: Ripe for Antitrust Challenge?*, ANTITRUST HEALTH CARE CHRON., Jan. 2012, at 26, 33–35, https://www.wsgr.com/PDFSearch/silber0112.pdf [https://perma.cc/7RJ8-8JQP] (describing the delay mechanisms used by GSK).

$185 million.[144] Thus, even with the settlement, the delay may have been worth $2.3 billion.

This Part continues with a discussion of the Generation 3.0 delay strategies that make up the toolbox for a branded pharmaceutical manufacturer, starting with perhaps the most well-known: product hopping and evergreening.

B. Product Hopping and Evergreening

Commentators have written for some time on the phenomenon known as evergreening, in which a company tries to refresh its market monopoly by making slight modifications to the delivery mechanism, dosage, or other characteristics to make the drug eligible for additional exclusivity or patents.[145] As described above, Generation 3.0 strategies involve active obstruction of generic entities, rather than side deals. One of the first Generation 3.0 strategies involves a variant of evergreening called "product hopping."

The following steps make up a product hop. First, the brand-name drug company makes a small change to its existing drug, right as its patents or regulatory exclusivities are about to expire, and introduces the new formulation as an entirely new drug. This new form is generally protected by new patents corresponding to the minor changes. The move forces a market shift away from the old drug—just as it is approaching its patent cliff.

The brand-name drug company brings about the market shift in a number of ways. Notably, the brand-name company usually undertakes a significant promotion and advertising campaign to herald the benefits of the "new" medication and push doctors to write prescriptions for the new drug. This strategy obstructs generic substitution in different ways, depending on the nature of the product hop. When the product hop involves a shift to an entirely new drug (e.g. a shift from Prilosec to Nexium in the market for heartburn relief and other stomach acid-related conditions, as described below), convincing doctors to prescribe the new drug prevents generic substitution simply because there is no generic equivalent.

Alternatively, in the case in which the product hop involves a switch to a new form of the drug (e.g. a shift from Suboxone tablets to Suboxone film

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[144] Carolina Bolado, *Judge Approves $150M Flonase Antitrust Accord*, LAW360 (June 14, 2013, 6:57 PM), http://www.law360.com/articles/450443/judge-approves-150m-flonase-antitrust-accord [https://perma. cc/CT2U-B4DP]; Jonathan Randles, *Judge Gives Final OK To $35M GSK Flonase Settlement*, LAW360 (June 19, 2013, 5:00 PM), http://www.law360.com/articles/451604/judge-gives-final-ok-to-35m-gsk-flonase-settlement [https://perma.cc/VC39-DRS2].

[145] *See generally* FELDMAN, *supra* note 13, at 170–77; Carrier, *supra* note 2; Jessie Cheng, Note, *An Antitrust Analysis of Product Hopping in the Pharmaceutical Industry*, 108 COLUM. L. REV. 1471 (2008); Vikram Iyengar, *Should Pharmaceutical Product Hopping Be Subject to Antitrust Scrutiny?*, 97 J. PAT. & TRADEMARK OFF. SOC'Y 663 (2015); Steve D. Shadowen, Keith B. Leffler & Joseph T. Lukens, *Anticompetitive Product Changes in the Pharmaceutical Industry*, 41 RUTGERS L.J. 1 (2009).

strips, as described below, in Section C), pharmaceutical representatives often ask physicians to append a note to their prescriptions asking the pharmacist to "Dispense as Written."[146] This prevents pharmacists from dispensing the generic version of the old form of the drug since the doctor has specifically requested the new form—a form for which there is no generic substitute.

Meanwhile, the brand-name company provides a monetary incentive to drug payors—including insurers, managed care organizations, and pharmaceutical benefit managers—to catalyze the product hop.[147] The new drug is often introduced with significant rebates and discounts to insurers, causing these insurers to prefer the use of the new drug over the old form in the short-term.[148] An insurer may even place the new drug in a preferred position in its formulary of drugs covered for patients—meaning that the patient co- pay for the new drug is likely to be lower compared to that of the old form. Thus, pressure for doctors to prescribe the new drug comes from all sides: from pharmaceutical reps preaching the benefits of the product hop, from patients wishing to minimize their co-pay, from insurers who have a short- term financial incentive to prefer the new drug, and from pharmacists who recognize the preferential place of the new drug on formularies and ask doctors to change prescriptions to the new drug even when the old form is prescribed.[149]

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[146] See Genentech's "Preserve Your Branded Choice" website for CellCept (a drug that prevents organ rejection after transplants), which heavily encourages healthcare professionals to write "Dispense as Written" on prescriptions so branded CellCept is dispensed. The website even includes a separate PDF file for all fifty states, the District of Columbia, Guam, and Puerto Rico, with specific information about the "Dispense as Written" guidelines in each jurisdiction. *Preserve Your Branded Choice*, CELLCEPT, http://www.cellcept.com/hcp/prescrib-ing-branded-cellcept [https://perma.cc/ATX8-PEA9].

[147] For some further discussion of this issue, see Shadowen, Leffler & Lukens, *supra* note 145, at 17–21.

[148] Note that these rebates are really only valuable to the insurer when you compare the price of the brand's "old drug" to the rebated/discounted price of the new drug. The cheapest option for the insurer would be to pay for a generic version of the old drug at a price cheaper than even a discounted version of a patent-protected new formulation. Further, rebates and discounts are likely to disappear or diminish once the product hop is sufficiently completed. [149] Consumers often receive financial incentives on top of differential co-pays. Many pharmaceutical companies provide co-pay "coupons" or "rebates" to patients. These incentives discount the patient's out-of-pocket costs for drugs at the point of sale, perhaps influencing the patient to purchase expensive drugs while shifting all cost (and risk) onto insurers. The economic implications of these coupons are an ongoing subject of debate in pharmaceutical pricing. Massachusetts was the only state to have banned these coupons until its law was repealed (for drugs without generic equivalents) in 2012, and federal health insurance (e.g. Medicare, Medicaid, veterans' benefits) users are ineligible for coupon benefits under anti-kickback laws. *See* David Schultz, *Drug Coupons: A Good Deal For The Patient, But Not The Insurer*, KAISER HEALTH NEWS (Oct. 1, 2012), http://khn.org/news/drug-coupons/ [https://perma.cc/D6Y3-SMPC] (noting laws preventing those on federal health insurance from using coupons and detailing the debate over co-pay rebates); Karen Weintraub, *Mass., 50th State, Now Allows Drug Coupons: What You Need To Know*, WBUR (July 16, 2012, 9:40 AM), http://commonhealth.wbur.org/2012/07/drug-coupons-massachusetts [https://perma.cc/3AFV-P8KT] (covering repeal of Massachusetts's drug coupon law). As of February 2016, CellCept, the drug described in note 146, provided a co-pay card to consumers, along with the push for

To complete the product hop, brand-name companies will often discontinue the previous version of the drug, closing distribution channels and sometimes even buying back all remaining inventory of the drug.[150] In some cases, the original drug is eventually removed or excluded from the insurance formularies or national databases used to determine generic equivalence, such as First Databank MedKnowledge, formerly known as (and still often referred to as) the National Drug Data File.[151]

When the original branded drug is excluded from formularies, use of an equivalent generic generally comes to a full halt. Substitution cannot take place because there is no longer a brand-name drug for the generic on the market. Even if a doctor were to write a prescription specifically for the generic instead of the new branded drug, most insurance companies will consider the generic drug to be a "branded" drug for co-pay and reimbursement purposes since it is the only drug on the market, which shifts more costs onto the consumer and discourages use of the drug.

In sum, the result is that a generic that was supposed to create competition for the original brand-name drug can no longer gain a foothold in the market. In a variant on this strategy, AstraZeneca switched the market from its original drug Prilosec to Nexium by moving Prilosec from a prescription medication to an over-the-counter drug,[152] and then shifting the prescription market to a newly patented Nexium. Commentators have argued that Nexium is little different from its predecessor drug.[153]

The strategy has been enormously successful. Before patent expiration, Prilosec was the country's number one selling drug with $6 billion per year in sales.[154] In 2013, twelve years after Nexium launched, Nexium was the number two selling drug with just under $6 billion in sales, $2.5 billion of

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doctors to prescribe the branded medication. *CellCept CoPay Card*, CELLCEPT, http://www.cellcept.com/hcp/patient-financial-resources/cellcept-copay-card [https://perma.cc/93H3-S2CA].

[150] *See* FELDMAN, *supra* note 13, at 175. In at least one instance, a pharmaceutical company "managed to persuade the FDA to withdraw its license" for an original branded drug right as generic competition was about to be permitted. Lars Noah, *Product Hopping 2.0: Getting the FDA to Yank Your Original License Beats Stacking Patents*, 19 MARQ. INTELL. PROP. L. REV. 161, 165 (2015).

[151] *See* Teva Pharm. USA, Inc. v. Abbott Lab., 580 F. Supp. 2d 345, 355 (D. Del. 2008) (featuring the case of TriCor, in which the brand-name manufacturer recoded earlier versions of TriCor as "obsolete" in the NDDF, allegedly blocking some substitution); *see also* Carrier, *A Real-World Analysis of Pharmaceutical Settlements*, *supra* note 2, at 1019–20 (discussing TriCor and the National Drug Data File).

[152] You might remember the omnipresent commercials featuring comedian "Larry the Cable Guy" trumpeting the news that Prilosec was available over-the-counter.

[153] *See* FELDMAN, *supra* note 13, at 171. Prescription Prilosec was not completely discontinued, but the move to over-the-counter availability created a product hop because insurers excluded Prilosec from their formularies once it became available without a prescription.

[154] *AstraZeneca Holds Off Rivals As Drug Patent Dies*, USA TODAY (Oct. 5, 2001), http://usatoday30.usatoday.com/money/general/2001-10-05-prilosec.htm [https://perma.cc/Y7AC-5YD6].

which is paid by the government and its beneficiaries under Medicare Part D.[155]

Other recent cases have even more alarming fact patterns. Consider Asacol, a drug used for the treatment of chronic ulcerative colitis. As the expiration of the Asacol patents approached and at least two generic companies planned to enter upon expiration, the brand-name manufacturer undertook a number of actions to extend its monopoly franchise.[156] First, it developed a higher-dose, extended-release version of the Asacol tablet.[157] The new version of Asacol received two new patents, which will both expire in 2021.[158] The company then attempted a product hop before the 2013 expiration of the Asacol patents through a marketing and promotion campaign. However, the new form of Asacol was only approved for moderately active ulcerative colitis.[159] The older form of Asacol was approved for both the moderate form and the mild form of the disease.[160] Thus, despite continued efforts to switch all patients to the new form and multiple complaints alleging that this represented unlawful off-label marketing (because the drug was not approved for all patients), the new form did not gain substantial market share.[161]

The company was not deterred. With Asacol's patent expiration approaching, the brand-name firm developed and introduced Delzicol, a 400mg tablet that was bioequivalent to Asacol.[162] In fact, as Internet commenters discovered, Delzicol was merely an Asacol tablet surrounded by a cellulose capsule.[163] If the capsule was cut open, the original Asacol tablet fell out.[164] Delzicol did not receive a new grant of exclusivity from the FDA because it was not considered a new molecular entity.[165] Nevertheless, the capsule allowed the company to obtain a patent—despite the fact that the capsule provides no additional therapeutic benefit.[166]

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[155] *U.S. Pharmaceutical Sales 2013*, *supra* note 135; Katie Thomas & Robert Pear, *Medicare Releases Detailed Data on Prescription Drug Spending*, N.Y. TIMES (Apr. 30, 2015), http://mobile.nytimes.com/2015/05/01/business/medicare-releases-detailed-data-on-prescription-drug-spending.html [https://perma.cc/XU5Y-VB7P].

[156] End-Payor Plaintiffs' Class Action Complaint at paras. 115–18, Teamsters Union 25 Health Servs. & Ins. Plan v. Allergan, PLC, No. 15-cv-12730, 2015 WL 3856331 (D. Mass. June 22, 2015).

[157] *Id.* at paras. 38–41.

[158] *Id.* at para. 40.

[159] *Id.* at para. 39.

[160] *Id.*

[161] *Id.* at paras. 52–57

[162] *Id.* at paras. 72–75.

[163] *Id.* at paras. 85–88.

[164] *Id.* at paras. 84–87.

[165] See Part II above for a discussion of this FDA non-patent exclusivity that provides marketing protection for new drugs with new active ingredients.

[166] Backing this point up is the fact that Delzicol was approved by the FDA as bioequivalent to Asacol, so it could not have been "medically superior" in any way. End-Payor Plaintiffs' Class Action Complaint, *supra* note 156, at para. 81. Given that the active ingredients of Asacol must be released in the gastrointestinal tract to have an effect, Asacol tablets have always been covered with an enteric coating that prevents the pill from breaking down in

The company argued that the change was necessary because a slight modification was also made to an inactive coating ingredient that may have posed safety concerns.[167] According to a complaint, however, this ingredient remains part of Asacol tablets sold in other countries, and switching out only this ingredient would not have led to additional exclusivity for Asacol.[168] Thus, this switch may have merely been subterfuge to display concern with safety, when the real reasoning was to add the patentable but inoperable cellulose capsule and maintain the company's supra-competitive profits.

Finally, the company went for the hard switch—it completely removed Asacol from the market, sending all patients to the other form of Asacol or to Delzicol. In a candid conference call, the company's CEO left no doubts about the strategy: "It's a hard conversion. We're stopping—we're going to stop the shipment of Asacol 400 shortly, and it will be all Delzicol. I think they're all familiar with what's going on."[169] The complaint also alleges the involvement of reverse payments and citizen petitions, offering an example of how "multiplicity tactics" are often involved in generic delay.[170]

Perhaps the most notable recent case in the product-hopping space is the case that may eventually bring about its downfall. Litigation over a product hop involving Namenda, an important Alzheimer's treatment, reached the Court of Appeals for the Second Circuit in spring 2015.[171] In a May decision, a three-judge panel denied drug manufacturer Actavis' appeal of a preliminary injunction that forced the company to continue selling the old drug alongside its newer product, Namenda XR.[172]

The old form of Namenda is a twice-a-day treatment for moderate-to-severe Alzheimer's. In July 2013—notably, three years after its approval by the FDA—Actavis introduced Namenda XR, a higher-dose treatment that could be taken once daily.[173] In August 2014, about one year before patents would expire on Namenda IR, Actavis tried to completely pull the old form of the drug from the market. One month later, the New York Attorney General's office filed a complaint alleging antitrust violations under the Sherman Act and sought a preliminary injunction to force Actavis to continue selling the older formulation. The FTC received the requested injunction in December 2014, and the decision was eventually upheld by the Second Circuit.[174]

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highly acidic stomach acid. Yet a complaint alleges that the cellulose capsule in Delzicol easily and quickly dissolves in stomach acid—thus it has no effect on drug delivery. *Id.* at paras. 80–82.

[167] *Id.* at paras. 89–103.

[168] *Id.* at para. 83.

[169] *Id.* at para. 108 (citing *Warner Chilcott Management Discusses Q4 2012 Results—Earnings Call Transcript*, SEEKING ALPHA (Feb. 22, 2013, 11:50 AM), http://seekingalpha.com/article/1216961-warner-chilcott-management-discusses-q4-2012-results-earnings-call-transcript [perma.cc/6A9D-6QJ5]).

[170] *Id.* at paras. 62–64.

[171] New York *ex rel.* Schneiderman v. Actavis PLC, 787 F.3d 638 (2d Cir. 2015).

[172] *Id.* at 643.

[173] *Id.* at 647–48.

[174] *Id.* at 649–50.

Actavis is important, and not just because it was one of the first cases in which product hopping was found to be potentially anticompetitive. Most important, the Namenda product hop took place in a market that the company completely dominated; Namenda is the only treatment in its class avail- able for Alzheimer's and the only treatment approved for moderate-to-severe Alzheimer's.[175] Thus, unlike other cases of product hopping where other drugs might be available as an inexact substitute, switching to Namenda XR was the only choice for Alzheimer's patients who completely depend on the treatment.[176]

Further, while the company appeared to be offering the benevolent innovation of a once-daily medication, all other Alzheimer's treatments had already moved to a once-a-day treatment before the introduction of Namenda XR.[177] The actions raise questions of whether Actavis had waited to incorporate a known innovation in order to thwart generic entry. Those allegations are heightened by the fact that Actavis failed to introduce the once-a-day form for three years after it was approved by the FDA, timed to less than a year before the patents on original Namenda would expire.[178]

The development of antagonist strategies such as product hopping has created the opportunity for brand-name firms to dip back into their pool of Generation 2.0 tactics. In particular, product hopping has spawned a new set of "boy scout" clauses, in which the brand-name drug company agrees to refrain from antagonistic behavior.[179] One such clause is an agreement not to product hop before generic entry, or to handsomely pay the generic if product hopping occurs. For example, in *In re Opana*, class action plaintiffs allege that Endo, a brand-name firm, agreed to pay a first-filing prospective generic what amounted to over $102 million, but only if sales of the brand-name drug fell below a certain level in the quarter before the generic launch date.[180] In exchange, the generic delayed its entry for over two years.[181] However, this significant drop in sales would likely occur only if there was a product hop away from the brand-name drug; thus, the agreement essentially

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[175] *See Current Alzheimer's Treatments*, ALZHEIMER'S ASS'N, http://www.alz.org/research/science/alzheimers_disease_treatments.asp [http://perma.cc/E66C-WGLX] (noting that memantine, the drug name for Namenda, is the only NMDA receptor antagonist treatment for Alzheimer's and was the only treatment approved for moderate-to-severe Alzheimer's at the time of the product hop). A newly introduced drug approved for moderate-to-severe Alzheimer's, Namzaric, combines memantine with donepezil, a cholinesterase inhibitor that had already been approved for Alzheimer's treatment in the United States in 1996. *Id.* The combination drug, however, is also sold by Actavis.

[176] *Actavis PLC*, 787 F.3d at 654 n.27.

[177] *Id.* at 647; New York v. Actavis PLC, No. 14 Civ. 7473, 2014 WL 7105198, at *34 (S.D.N.Y. Dec. 11, 2014) (granting preliminary injunction).

[178] *Actavis PLC*, 787 F.3d at 647–48.

[179] See Section IV.C for more discussion of "boy scout" clauses.

[180] End-Payors Plaintiffs' Consolidated Amended Class Action Complaint at para. 2, *In re* Opana ER Antitrust Litig., No. 14 C 10150, 2015 WL 2182959 (N.D. Ill. May 4, 2015).

[181] *Id*.

functioned as a promise to pay the generic in the event Endo decided to product hop.[182]

On its face, this agreement appears to actually promote competition by deterring a brand-name from product hopping before the generic could enter. The circumstances of the *Opana* settlement, however, were designed to actually effectuate Endo's product hop. Complainants allege that the two companies knew before entering into the agreement that the brand-name company would product hop—and in fact, Endo began the FDA approval process for a new version of the brand-name drug just one month after the agreement.[183] Therefore, knowing that a product hop was coming, the $102 million payment effectively served as a simple reverse payment to the generic in return for delaying entry until Endo had a chance to complete its product hop.[184] By the time the generic launched, ninety percent of the product's market had already switched to the new formulation.[185] In sum, Endo's boy scout clause was only one part of a strategy in which a product hop triggered a side deal that essentially served as a reverse payment for delay. Put another way, Endo's generous invocation of Scout's honor was in fact an excuse to use a new Generation 3.0 strategy to enter into a Generation 2.0 deal masking a simple Generation 1.0 reverse payment. The weapons may differ—and may be used simultaneously—but the games remain the same.

C. REMS-based Delay

REMS-based delay is another strategy in the Generation 3.0 obstruction toolkit. REMS (Risk Evaluation and Mitigation Strategies) are risk management and safety plans that the FDA can require a pharmaceutical company to implement beyond the standard labeling requirements that apply to most drugs.[186] Such plans are developed by the pharmaceutical company and then approved and continuously reviewed by the FDA.[187]

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[182] *Id*. at paras. 3, 143–52.

[183] *Id*. at para. 3.

[184] *Id*. at para. 149.

[185] *Id*. at para. 158. The generic also secured a no-AG agreement with regards to Opana ER as well as other side deal considerations, allowing it to recover some of the profits it lost by allowing a product hop. In the absence of the settlement, the generic may have faced competition from an Endo authorized generic when it launched. Instead, it was able to launch as the sole generic product although it faced a market that had shifted to a new version of Opana. The no-AG agreement also helped to make the deal worthwhile for the generic even in the case where Endo failed to product hop and did not trigger the $102 million payment. *Id*. at paras. 156–57.

[186] REMS, which stands for "Risk Evaluation and Mitigation Strategies," is a system introduced by the FDA in 2007 as part of amendments to the FDA Act in 2007. U.S. FOOD & DRUG ADMIN., FDA BASICS WEBINAR: A BRIEF OVERVIEW OF RISK EVALUATION AND MITIGATION STRATEGIES (REMS) 2 (Aug. 12, 2015), http://www.fda.gov/downloads/AboutFDA/Transparency/Basics/UCM328784.pdf [https://perma.cc/T6F5-2ZC2] (presenting risk evaluation and mitigation strategies).

[187] *Id*.

REMS are unique to a particular drug, but they can include the following elements: additional medication inserts to be included with the drug, a campaign or "communication plan" to inform key stakeholders about the risks of the drug, and, most notably, "Elements to Assure Safe Use" ("ETASU").[188] ETASU are the most restrictive requirement of a REMS pro- gram because they directly influence how and when the drug can be used. ETASU can include elements such as patient monitoring or testing while taking the drug, special certification for prescribers or pharmacies, or limitations on how and where the drug can be dispensed (e.g. only in a hospital or certified infusion site).[189] REMS can be modified or completely withdrawn after further assessment.[190]

The number of new requirements that REMS can impose on the sale, distribution, or marketing of a drug have made it ripe for abuse by branded drug manufacturers looking to keep generics out of the market. For example, a common ETASU restricts sales of a particular medication to hospitals and specially certified pharmacies. This creates an obstacle for would-be generic manufacturers looking for generic approval. The generic must prove that it is bioequivalent to the brand-name drug,[191] and testing for bioequivalence requires that the generic applicant use the brand-name drug as a comparison to the generic formulation.[192] Therein lies the problem. A number of cases have involved complaints that the brand-name drug company refused to sell a small amount of their drug to the generic on the grounds that the FDA limits the drug's distribution to specific outlets, and the generic company is not one of those outlets. As described below, the brand-name company refuses, even as the FDA insists that the company is free to sell to the generic hopeful.

Actelion was one of the first cases on this subject when it was filed in 2012.[193] The brand-name company refused to provide samples of two drugs to potential generic companies, which prevented the generic hopefuls from filing their applications.[194] The brand-name company's position is difficult to fathom. Congress considered the potential for this type of tactic, and the legislation establishing REMS includes a provision specifically stating that an ETASU cannot be used to block or delay approval of a generic.[195] Further,

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[188] *Id*.

[189] *Id*.

[190] *Id*.

[191] 21 U.S.C. § 355(j)(2)(A)(iv) (2012).

[192] 21 U.S.C. § 355(j)(8) (2012).

[193] Actelion Pharm. LTD v. Apotex Inc., No. 12-5743, 2013 WL 5524078 (D.N.J. Sept. 6, 2013); *see also* Kat Greene, *Actelion Settles Row Over Giving Drugs to Generic Makers*, LAW360 (Feb. 28, 2014, 7:07 PM), http://www.law360.com/articles/514434/actelion-settles-row-over-giving-drugs-to-generics-makers [http://perma.cc/9A4R-BESB]. In one other previous case filed in 2008, Lannett accused Celgene of refusing to provide it samples of Thalomid. The case ended in a settlement. Verified Complaint for Mandatory Injunctive Relief, Declaratory Relief and Money Damages, Lannett Co., Inc. v. Celgene Corp., No. 08-3920, 2011 WL 1193912 (E.D. Pa. Aug. 15, 2008).

[194] *Actelion Pharm.*, 2013 WL 5524078, at *1.

[195] 21 U.S.C. § 355–1(f)(8) (2012).

the FDA has repeatedly said that brands may sell samples to firms for bioequivalence testing without violating their REMS program, even issuing letters to branded manufacturers specifically permitting them to give samples to prospective generics.[196] The legal arguments in the *Actelion* case focused on whether or not there is a duty to deal on the part of the brand-name company and whether refusal to deal constitutes an antitrust violation.[197] Actelion asserted that it has a right to refuse sale even in the absence of the REMS, while the FTC filed a brief stating that the company's action may amount to exclusionary conduct.[198] The case ended in a settlement in early 2014.[199]

In a similar case filed against brand-name drug manufacturer Celgene, a generic hopeful alleged that it spent five years trying unsuccessfully to get a sample of Celgene's Thalomid and another five years trying unsuccessfully to obtain a sample of Celgene's Revlimid.[200] Although the judge dismissed some claims in the generic's complaint, she allowed important antitrust claims to survive a motion to dismiss, finding that the generic pleaded with enough detail that Celgene had no "legitimate business reasons" for denying samples.[201]

REMS manipulation, in theory, could be particularly dangerous for generic competition. REMS are not linked to patent protection and can con-

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[196] *See* CTR. FOR DRUG EVALUATION & RES., U.S. FOOD & DRUG ADMIN., RISK EVALUATION AND MITIGATION STRATEGY (REMS) PUBLIC MEETING 270–72 (July 28, 2010)(statement by Jane Axelrad, Associate Director of Policy, Ctr. for Drug Evaluation and Res.), http://www.fda.gov/downloads/Drugs/NewsEvents/UCM224950.pdf [https://perma.cc/V22K-99B7] (asserting that REMS should not be a barrier to acquiring generic samples). In part, these letters came about after a citizen petition filed in 2009 by Dr. Reddy's asking the FDA to issue guidance regarding the use of REMS to block or delay generic entry. It also asked the FDA to establish a procedure by which the FDA would provide letters on behalf of generic applicants to explain that the generic will meet the REMS safe use requirements that might be implicated in bioequivalence testing. *See* Citizen Petition from Kumar Sekar, Senior Dir., to Div. of Dockets Mgmt., U.S. Food & Drug Admin., No. FDA-2009-P-0266-0001, at 10 (June 10, 2009), http://www.fdalawyersblog.com/Dr_Reddys_Laboratories,_Inc_-_Citizen_Petition.pdf [https://perma.cc/95H9-5KXL]. Dr. Reddy's was attempting to obtain samples of Celgene's Revlimid and Thalomid, which are also the subject of another ongoing REMS-based lawsuit.

[197] *See generally* Darren S. Tucker, Gregory F. Wells & Margaret Sheer, *REMS: The Next Pharmaceutical Enforcement Priority?*, 28 ANTITRUST 74 (2014).

[198] For a detailed analysis of the potential antitrust issues in restricted distribution cases, see Michael A. Carrier, Nicole L. Levidow & Aaron S. Kesselheim, *Using Antitrust Law to Challenge Turing's Daraprim Price Increase*, 31 BERKELEY TECH. L.J. (forthcoming 2016), http://ssrn.com/abstract=2724604 [https://perma.cc/BAG9-3EKY].

[199] Greene, *supra* note 193; Lance Duroni, *Actelion Denied Judgment in Tracleer Antitrust Suit*, LAW360 (Oct. 21, 2013, 8:00 PM), http://www.law360.com/articles/481879 [http://perma.cc/SU7D-S4WV]. Although a settlement may represent a party's rational calculation of the strength of its case and the costs of continuing to litigate, it may also represent the strategic choice to abandon a case or pay off the other side if damaging information might emerge or dangerous precedents might be set.

[200] Mylan Pharmaceuticals v. Celgene Corp., No. 14-cv-2094, Transcript of Oral Opinion at *4–9 (D.N.J. Dec. 22, 2014) (denying in part and granting in part Celgene's motion to dismiss by oral opinion). The case later ended in a settlement.

[201] *Id.* at *17–18; *see also* Carrier, Levidow & Kesselheim, *supra* note 198, at *13–14 (discussing this case).

tinue indefinitely, even after the expiration of all exclusivities.[202] Thus, if a company, hiding behind a restrictive REMS, refuses to allow samples to generic hopefuls, the brand-name company could continue its monopoly past the end of the patent term. Even if the company is eventually forced to share samples, as described above, every month of delay is valuable.

Furthermore, a restricted distribution scheme does not even need a REMS (or an active patent) to be effective in blocking generic competition. For example, in September 2015, Turing Pharmaceuticals and its founder, Martin Shkreli, became the subject of intense scrutiny after raising the price of a drug by almost 5,500%.[203] Turing had bought the rights to Daraprim (pyrimethamine), an antimalarial drug also used for treatment of infections common in HIV-positive patients, for $55 million. The company then immediately raised the price of the drug from $13.50 a tablet to $750 a tablet.[204] A thirty-day course of the drug became $20,000, rather than just $400 before the increase.

The mere magnitude of the price increase for a potentially life-saving drug—and one that had already been off-patent for decades—led to immediate public outrage, causing Shkreli to eventually promise a price reduction.[205] Behind the price increase, however, was also a REMS-like tactic meant to block potential generic competition. When Turing acquired the rights to Daraprim, it maintained a restricted distribution system originally put in

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[202] For example, all forms of clozapine, a drug for schizophrenia treatment, are covered by a REMS that requires blood testing and pharmacy certification, among other restrictions. *Approved Risk and Mitigation Strategies (REMS): Clozapine*, U.S. FOOD & DRUG ADMIN. (Sept. 15, 2015), http://www.accessdata.fda.gov/scripts/cder/rems/index.cfm?event=RemsDetails.page&REMS=351 [http://perma.cc/27ZK-HVCB]. The original patents on clozapine have expired and numerous generics are now available on the market. New orally disintegrating tablets have remaining patent exclusivity, but those patents are on the specific product and not the "substance" of clozapine. *Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations*, U.S. FOOD & DRUG ADMIN. (Feb. 9, 2016), http://www.accessdata.fda.gov/scripts/cder/ob/docs/queryai.cfm [https://perma.cc/NHZ9-4LV6] (search for "Clozapine" in the active ingredient field).

[203] Andrew Pollack, *Drug Goes From $13.50 a Tablet to $750, Overnight*, N.Y. TIMES (Sept. 20, 2015), http://www.nytimes.com/2015/09/21/business/a-huge-overnight-increase-in-a-drugs-price-raises-protests.html [http://perma.cc/F26V-JSKR]. The price of the drug was as low as $1 in 2010, before a series of acquisitions. *Id*.

[204] *Id*.

[205] Andrea Mitchell & Phil Helsel, *Drug CEO Will Lower Price of Daraprim After Hike Sparked Outrage*, NBC NEWS (Sept. 23, 2015), http://www.nbcnews.com/news/us-news/drug-ceo-will-lower-price-daraprim-after-outrage-n431926 [http://perma.cc/9FT4-CBAV]. Further, in October 2015, Imprimis Pharmaceuticals announced that it would sell 100-count bottles of pyrimethamine mixed with leucovorin for under $100. As a compounding pharmaceutical company, the formulations are not FDA approved or subject to generic substitution, but they can be made available to patients by direct prescription from a physician. *See* Press Release, Imprimis Pharm., Imprimis Pharmaceuticals to Make Compounded and Customizable Formulation of Pyrimethamine and Leucovorin Available for Physicians to Prescribe for their Patients as an Alternative to Daraprim (Oct. 22, 2015), http://imprimispharma.investorroom.com/2015-10-22-Imprimis-Pharmaceuticals-to-Make-Compounded-and-Customizable-Formulation-of-Pyrimethamine-and-Leucovorin-Available-for-Physicians-to-Prescribe-for-their-Patients-as-an-Alternative-to-Daraprim [http://perma.cc/3PFG-UA2W].

place by Impax, the previous owner.[206] As discussed earlier in this section, restricted or controlled distribution is often a requirement of a REMS when a drug presents special concerns regarding safety, administration, or storage. Yet Impax (and later, Turing) seems to have instituted a restricted distribution system for no safety reason whatsoever, making the drug only available through Walgreen's Specialty Pharmacy.[207] Along with creating access problems for hospitals,[208] the move in part seemed to be designed to make it difficult for generics to gain access to samples.[209]

Comments from Turing executives support this implication. In response to the Daraprim pricing controversy and the potential for generic competition, Jon Haas, director of patient access at Turing, said the following: "Most likely I would block that purchase [by a generic]. We spent a lot of money for this drug. We would like to do our best to avoid generic competition. It's inevitable. They seem to figure out a way [to make generics], no matter what. But I'm certainly not going to make it easier for them."[210] The comments suggest a concerted effort to block generic competition, and a failure to accept the intent of the Hatch-Waxman's system for introduction of generic drugs. In addition, although Turing executives may have spoken more directly than others, actions in many corners of the pharmaceutical industry reflect a similar mindset. Turing's actions, specifically the use of restricted distribution to block competition, are now under investigation by the New York attorney general.[211] U.S. lawmakers have also called on the FTC to look into the Turing business model.[212]

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[206] Michael Carrier & Aaron Kesselheim, *The Daraprim Price Hike And A Role For Antitrust*, HEALTH AFF. BLOG (Oct. 21, 2015), http://healthaffairs.org/blog/2015/10/21/the- daraprim-price-hike-and-a-role-for-antitrust/ [http://perma.cc/3Z7V-DQ6C].

[207] *Id*.

[208] Letter from Stephen B. Calderwood, President, Infectious Diseases Soc'y of Am., and Adaora Adimora, Chair, HIV Medicine Ass'n, to Tom Evegan, Head of Managed Markets, Turing Pharm., and Kevin Bernier, Nat'l Dir. of All. Dev. & Pub. Affairs, Turing Pharm. (Sept. 8, 2015), http://www.hivma.org/uploadedFiles/HIVMA/HomePageContent/PyrimethamineLetterFINAL.pdf [http://perma.cc/F2ZV-XPBK].

[209] Carrier, Levidow & Kesselheim, *supra* note 198.

[210] Ed Silverman, *How Martin Shkreli Prevents Generic Versions of His Pricey Pill*, STAT PHARMALOT (Oct. 5, 2015), http://pharmalot.com/how-martin-shkreli-prevents-generic-versions-of-his-pricey-pill/ [http://perma.cc/U78B-U6YE].

[211] Andrew Pollack, *New York Attorney General Examining Whether Turing Restricted Drug Access*, N.Y. TIMES (Oct. 12, 2015), http://www.nytimes.com/2015/10/13/business/new-york-attorney-general-examining-if-turing-restricted-drug-access.html [http://perma.cc/CTF6-DSNL].

[212] *Id*. In December 2015, Shkreli was arrested on charges of securities fraud based on actions at previous companies and later resigned as CEO of Turing. Christopher M. Matthews, Rob Copeland & Rebecca Davis O'Brien, *Martin Shkreli, Pharma Executive, Arrested on Fraud Charges*, WALL. ST. J. (Dec. 17, 2015), http://www.wsj.com/articles/martin-shkreli-ar- rested-on-fraud-charges-1450359637 [http://perma.cc/WA34-CAFL]; Press Release, Turing Pharm. AG, Turing Pharmaceuticals AG Announces Appointment of Ron Tilles as Interim CEO (Dec. 18, 2015), http://www.turingpharma.com/media/press-release?headline=turing-pharmaceuticals-ag-announces-appointment-of-ron-tilles-as-interim-ceo [http://perma.cc/U6H7-HHHG].

As Carrier, Levidow, and Kesselheim have detailed, the Daraprim system was not the first time a Skhreli-led company implemented a restricted distribution system.[213] Notably, Skhreli's previous company, Retrophin, bought the rights to a rare kidney-disorder drug called Thiola. Retrophin increased the price of the drug 2000% from $1.50 to $30 a pill, but it also created a still-active closed distribution system known as "Thiola Total Care."[214] This system requires a patient and the patient's doctor to fax enrollment forms to Retrophin, which then manages direct shipments not through an online system but only over the phone.[215] Documents that Turing turned over to Congress in advance of a February 2016 hearing revealed that, internally, it was known that "[e]xclusivity (closed distribution) creates a barrier and pricing power."[216]

Restricted distribution schemes, whether they involve a REMS or not, also may be deployed to prevent generic substitution by pharmacists. In another story that captured the public's attention, federal prosecutors announced an investigation of Valeant Pharmaceuticals, also pilloried for acquiring medicines and then substantially increasing prices.[217] That accusation, however, was only the first of a series of allegations that would unfold against Valeant. Just days later, journalists discovered that Valeant had a deep relationship with a specialty pharmacy known as Philidor that essentially only filled prescriptions for Valeant's drugs and dermatology creams.[218] This investigation in turn led to the discovery of numerous pharmacies and subsidiaries covertly linked to Valeant.[219]

The link between Valeant and specific specialty pharmacies allowed Valeant to ensure that its drugs were filled instead of generic prescriptions. Doctors would submit prescriptions for Valeant drugs to a mail-order spe-

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[213] *See* Carrier, Levidow & Kesselheim, *supra* note 198, at *20–21.

[214] *Id.*

[215] *Thiola Total Care Hub*, THIOLA, http://www.thiola.com/hub [http://perma.cc/2JQ6-TAA2]. Notably, although it may be a technical error, the enrollment form on the Total Care Hub website automatically fills in the bubble for "dispense as written." *Patient Enrollment Form for Thiola Total Care Hub*, THIOLA, http://www.thiola.com/assets/pdf/THI010V2.pdf [https://perma.cc/C6LY-64Q3].

[216] *See* Carrier, Levidow & Kesselheim, *supra* note 198, at *21 (citing Memorandum from Democratic Staff to Democratic Members of the Full H. Comm. on Oversight and Gov't Reform Regarding Documents Obtained by Comm. from Turing Pharm. 3 (Feb. 2, 2016), http://democrats.oversight.house.gov/sites/democrats.oversight.house.gov/files/documents/Memo%20on%20Turing%20Documents.pdf [https://perma.cc/C2KH-XSXY]).

[217] Jonathan D. Rockoff, *Valeant Pharmaceuticals Under Investigation by Federal Prosecutors*, WALL ST. J. (Oct. 15, 2015), http://www.wsj.com/articles/valeant-pharmaceuticals-under-investigation-by-federal-prosecutors-1444874710?mod=e2tw [http://perma.cc/ZFY9-D5AL].

[218] Roddy Boyd, *The King's Gambit: Valeant's Big Secret*, S. INVESTIGATIVE REPORTING FOUND. (Oct. 19, 2015), http://sirf-online.org/2015/10/19/hidden-in-plain-sight-valeants-big- crazy-sort-of-secret-story/ [http://perma.cc/N34K-B8TQ].

[219] Bertrand Marotte, *Valeant's Sales Network: Deciphering a Complex Web of Companies*, GLOBE & MAIL (Oct. 27, 2015), http://www.theglobeandmail.com/report-on-business/valeants-sales-network-the-firms-and-chess-terms-tied-to-it/article27009058/ [http://perma.cc/9D3F-9HJ8].

cialty pharmacy, the prescription would be sent to the patient, and then the pharmacy would work with insurance companies to secure reimbursement.[220] When the prescription is sent to a specialty pharmacy that only deals with specific drug brands, however, it is very unlikely that any substitution will take place to dispense a generic or over-the-counter medicine instead of the brand-name drug.[221] As another company using a similar business model disclosed in a regulatory filing, the mail-order prescriptions "are less likely to be subject to the efforts of traditional pharmacies to switch a physician's intended prescription of our products to a generic or over-the-counter brand."[222] That company, Horizon, reportedly charged $1,500 a month for a medication called Duexis that simply combined ibuprofen and the active ingredient in Pepcid.[223]

The brunt of the costs of this scheme falls on insurers and not patients, perhaps intentionally so that patients and doctors do not feel the sticker shock of high prices. Nevertheless, games like these certainly would not help lower insurance premiums, nor would they help rationalize national spending on health care. Moreover, when insurers balked at the high cost of Vale- ant prescriptions, Philidor and other pharmacies allegedly took drastic action to secure reimbursement, including modifying prescription codes to make it appear as if the doctor specifically requested that a prescription be "dispensed as written" with Valeant-branded medication.[224] As a result, these schemes continually blocked generic competitors from participating in the market for the medication.

Aside from restricted distribution programs, other REMS-based schemes have appeared as well. Frequently, a REMS program will ask a drug's manufacturers to develop a more detailed medication guide or a communication plan to inform doctors and patients about the elevated risks of a drug. For example, Gilenya (fingolimod), an immunosuppressant that treats relapses of multiple sclerosis, has a REMS that requires a communication plan with materials for doctors and patients, as well as an FDA-mandated pregnancy registry.[225]

When there are multiple manufacturers of a drug—for example, a brand and generic—the FDA often requires all parties to develop and agree on the same REMS program, known simply as a Single Shared REMS program

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[220] Andrew Pollack, *Drug Makers Sidestep Barriers on Pricing*, N.Y. TIMES (Oct. 19, 2015), http://www.nytimes.com/2015/10/20/business/drug-makers-sidestep-barriers-on-pricing.html?smid=pl-share [http://perma.cc/GV46-F5CN].

[221] *Id*.

[222] *Id*.

[223] *Id*.

[224] Caroline Chen & Ben Elgin, *Philidor Said to Modify Prescriptions to Boost Valeant Sales*, BLOOMBERG (Oct. 29, 2015), http://www.bloomberg.com/news/articles/2015-10-29/philidor-said-to-modify-prescriptions-to-boost-valeant-sales [http://perma.cc/Y4JW-4XKA].

[225] *See Approved Risk and Mitigation Strategies (REMS): Gilenya (fingolimod)*, U.S. FOOD & DRUG ADMIN. (May 14, 2015), http://www.accessdata.fda.gov/scripts/cder/rems/index.cfm?event=IndvRemsDetails.page&REMS=22 [http://perma.cc/27ZK-HVCB].

("SSRS").[226] In particular, generic entry can be conditioned on FDA approval of a SSRS. The idea that a brand-name company will be willing to cooperate in streamlining the approval of a generic seems optimistic at best. When brand name drug makers are able to delay entry by a refusal to cooperate, it is not a surprise that they have taken advantage of it, creating another form of generic delay. The generic cannot get its drug approved until the brand-name company cooperates, and the brand-name company avoids cooperating to keep the generic off the market. It could be compared to a high school group project where one member not only refuses to complete a fair share of the work but also has an incentive to see the project fail in order to sabotage the grades of fellow group members.

The most notable case dealing with this strategy is *In re Suboxone*.[227] Suboxone is used for the treatment of addiction to opioids, such as heroin and oxycodone.[228] The drug has saved the lives of many addicts, but with serious consequences. Suboxone has become a street drug of its own, and it comes with the risk of severe side effects and withdrawal symptoms.[229] Suboxone includes both a semi-synthetic opioid and a drug used to combat the effects of an opioid overdose (with unpleasant side effects), which is included for the sole purpose of deterring potential users from injecting the drug intravenously.[230]

Suboxone is perhaps the poster child for a drug needing a comprehensive REMS program. Its REMS program includes a medication guide, a checklist that physicians must follow when prescribing the drug, federal authorizations for prescribers, limits on how much medication can be initially prescribed, an intensive monitoring program requiring frequent patient return visits, and monitoring on the part of manufacturers, which can even include "surveillance" and "street ethnography" to detail patterns of abuse.[231]

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[226] *In re* Suboxone (Buprenorphine Hydrochloride and Naloxone) Antitrust Litig., 64 F. Supp. 3d 665, 675 (E.D. Pa. Dec. 3, 2014) (granting dismissal of some counts and in part denying some counts).

[227] *Id*.

[228] SUBOXONE, http://www.suboxone.com [http://perma.cc/PM5B-7ANB].

[229] *See* Deborah Sontag, *Addiction Treatment With a Dark Side*, N.Y. TIMES (Nov. 16, 2013), http://www.nytimes.com/2013/11/17/health/in-demand-in-clinics-and-on-the-street- bupe-can-be-savior-or-menace.html [http://perma.cc/K6CX-4JRA]; *Risk Evaluation and Mitigation Strategy for Suboxone*, INDIVIOR, http://www.suboxonefilmrems.com [http://perma.cc/ D7AV-H7J7].

[230] *See* Sontag, *supra* note 229.

[231] U.S. FOOD & DRUG ADMIN., RISK EVALUATION AND MITIGATION STRATEGY FOR SUBOXONE, RECKITT BENCKISER PHARMACEUTICALS, INC., NDA 20-733 (Dec. 2011), http://www.accessdata.fda.gov/drugsatfda_docs/rems/Suboxone%20sublingual%20tablets_2011-12-22_REMS%20DOCUMENT.pdf [http://perma.cc/ER4A-TEDR] (approving initial Risk Evaluation and Mitigation Strategy); *see* Sontag, *supra* note 229; *see also* Hyman, Phelps & McNamara PC, *Risk Evaluation and Mitigation Strategy Tracker*, FDA LAW BLOG (July 23, 2015), www.fdalawblog.net/fda_law_blog_hyman_phelps/files/REMS_Tracker.xls [https://perma.cc/7BSE-7GTH] (providing extensive tracking of REMS approvals).

Suboxone is also a blockbuster with over $1.55 billion in sales in 2012, linked to an explosion of painkiller and heroin abuse in the United States.[232] Thus, with the brand-name company, Reckitt Benckiser, nearing the end of its exclusivity for Suboxone tablets in 2009 and generic entry looming on the horizon, the company undertook an extraordinary set of actions to maintain a monopoly on the Suboxone franchise.[233] Complainants allege tactics including an anti-competitive product hop, sham citizen petitions, and REMS abuse.[234]

Specifically, as exclusivity was about to expire on Suboxone tablets, complaints allege that Reckitt began to develop a film version of Suboxone with the intention of product hopping from tablet to film form.[235] The timing was off for the company, however, because the final exclusivities for the tablet were scheduled to expire about eleven months before the FDA approved the film version.[236] The resulting eleven-month gap could have been a prime opportunity for a generic to enter and gain market share before the FDA approved the Suboxone film. To effectuate a product hop, complainants argue that the brand-name company undertook a massive sales and marketing campaign to "promote" the idea that the tablet version of Suboxone presented safety concerns, which would be alleviated by the Suboxone film version.[237] The campaign claimed that there was a high risk of pediatric over- dose from a bottle of Suboxone tablets, a risk remedied by the packaging for the film version because the films are packaged individually.[238] Notably, unit-dose packaged tablets are available in all other markets where Subox- one is sold, other than in the United States.[239] In other words, the problem

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[232] Sontag, *supra* note 229.

[233] Suboxone is now sold and distributed by Invidior, a specialty pharmaceutical company that Reckitt Benckiser spun off from its core business in 2014. Ashley Armstrong, *Reckitt Benckiser to Spin-Off Drug Unit Into New Listing*, TELEGRAPH (Nov. 17, 2014), http://www.telegraph.co.uk/finance/newsbysector/epic/rbdot/11235616/Reckitt-Benckiser-to-spin-off-drug-unit-into-new-listing.html [http://perma.cc/248G-T3M9].

[234] End Payor Plaintiffs' Consolidated Amended Class Action Complaint at paras. 3–5, *In re* Suboxone (Buprenorphine Hydrochloride and Naloxone) Antitrust Litig., No. 13-md-02445, 2013 WL 5467390 (E.D. Pa. Aug. 15, 2013).

[235] *Id.* at para. 15.

[236] *In re* Suboxone (Buprenorphine Hydrochloride and Naloxone) Antitrust Litig., 64 F. Supp. 3d 665, 674 (E.D. Pa. 2014).

[237] *Id.*

[238] End Payor Plaintiffs' Consolidated Amended Class Action Complaint, *supra* note 234, at paras. 23–26; *see also* U.S. FOOD AND DRUG ADMIN., NDA 20-733, SUBOXONE RISK EVALUATION AND MITIGATION STRATEGY (Dec. 2011), http://www.accessdata.fda.gov/drugsatfda_docs/rems/Suboxone%20sublingual%20tablets_2011-12-22_REMS%20DOCUMENT.pdf [https://perma.cc/ER4A-TEDR] (approving initial Risk Evaluation and Mitigation Strategy).

[239] End Payor Plaintiffs' Consolidated Amended Class Action Complaint, *supra* note 234, at paras. 21, 28. Further, it was argued that the film may exacerbate safety concerns regarding pediatric exposure. Since the film dissolves more quickly than the tablet, it may be difficult to prevent a child from being exposed to the medication once they put it in their mouth. Also, the potential for abuse may increase since the film's dissolvability can make its use more discrete. *In re Suboxone*, 64 F. Supp. 3d at 674; *see also* Sontag, *supra* note 229 ("'It's such a thin strip they'll put it in the Holy Bible, let it melt and eat a page right out of the good book,' said Ken Mobley, a jailer in Whitley County, Ky.").

could have been remedied with the tablets, but the company had not seen fit to provide that resolution in the U.S. market.

Despite the campaign, the possibility of generic tablet entry continued to be a problem for Reckitt. Thus, the company sent multiple letters and applications to the FDA proposing a REMS because of the risks of abuse and pediatric exposure.[240] This request was approved, and the FDA required that the generic and branded Suboxone share the same REMS.[241] Unsurprisingly, attempts at cooperation between Reckitt and the prospective generics proved unsuccessful. Eventually, the generics gave up, applying for and receiving a waiver to create a REMS without the branded drug company—the first time such a waiver had ever been granted.[242]

The nine-month period during which generics and the brand name company could not come to an agreement on a REMS may have been worth upward of $1 billion in Suboxone sales. This is an enormous sum to result from a disagreement presumably not over the medication itself, but on how its use would be monitored and how the risks would be explained to the public.[243]

In the resulting lawsuit, the judge in 2014 dismissed the generic company's standalone claim that Reckitt's actions regarding the REMS amounted to an antitrust violation.[244] The saga of *Suboxone* continues in the next sec-

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[240] Letter from Judith A. Racoosin, Deputy Dir. for Safety, Ctr. for Drug Evaluation & Research, to John Song, Manager, NA Regulatory Affairs Operations, at 1 (Dec. 22, 2011), http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2011/020733s007,s008ltr.pdf [https://perma.cc/LR5H-V2UM] (approving Risk Evaluation and Mitigation Strategy).

[241] *In re Suboxone*, 64 F. Supp. 3d at 675. This requirement is detailed in 21 U.S.C. § 355(i)(1) (2012).

[242] *In re Suboxone*, 64 F. Supp. 3d at 675–76; *see also* Kurt R. Karst, *In Case You Missed It . . . . We Did! Prometheus Takes Action Against FDA Over Generic LOTRONEX Approval and REMS Waiver, and Then Promptly Drops Case*, FDA LAW BLOG (June 24, 2015), http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2015/06/in-case-you-missed-it-we-did-prometheus-takes-action-against-fda-over-generic-lotronex-approval-and-.html [https://perma.cc/C5ML-XJAC] (noting that the Suboxone REMS waiver was the first granted by the FDA); *see also* Prometheus Lab. Inc. v. Burwell, No. 15-cv-00742 (D.D.C. filed May 18, 2015) (D.D.C. denied motion for temporary restraining order May 21, 2015. Prometheus dropped suit June 11, 2015 where a brand-name company filed suit against the FDA for granting a second REMS waiver in 2014.). The FDA responded by noting, in part, that the brand-name company "dragg[ed] its feet for more than three years rather than collaborate with [the generic]." *See* Federal Defendants' Opposition to Plaintiff's Motion for a Temporary Restraining Order And/Or Preliminary Injunction at 6, Prometheus Lab. Inc. v. Burwell, No. 15-cv-00742 (D.D.C. May 28, 2015), http://www.fdalawblog.net/LOTRONEX%20-%20Roxane%20TRO-PI%20 Opp.pdf [https://perma.cc/5A6J-AJZ7]. Less than a month later, Prometheus completely dropped its suit. *See* Karst, *supra*.

[243] Assuming $1.55 billion in sales of Suboxone in 2012. This assumes that the REMS delay was the only issue standing in the way of generic approval, which is not a fully unreasonable assumption. As will be discussed below, in Section D, immediately before the generics applied for a REMS waiver, Reckitt announced a withdrawal of Suboxone tablets from the market and filed a citizen petition asking for the generic ANDA to not be approved. Immediately after the citizen petition was dismissed in early 2013, the ANDAs were approved. Thus, it is possible that generic entry could have been approved immediately after the REMS waiver was approved had Reckitt not taken further action.

[244] *In re Suboxone*, 64 F. Supp. 3d at 688.

tion, however, with further complaints of anticompetitive behavior.[245] In short, it is clear that although the FDA would like to get "[all the parties] to play nicely together"[246] on the playground, mere talk is unlikely to achieve this goal when billions are on the line. As the FDA admitted in another REMS case, the agency simply lacks an effective mechanism to force the two parties to reach agreement.[247]

D. Delay via Citizen Petition

Citizen petitions offer another way to create obstacles to generic entry. Since 1979, the FDA has allowed the public to request that the agency "issue, amend, or revoke a regulation or order or take or refrain from taking any other form of administrative action."[248] Although the program applies to all products under the FDA's jurisdiction, the majority of citizen petitions are related to pharmaceuticals, rather than food, cosmetics, or medical devices.[249]

Many pharmaceutical petitions are relatively benign. A number ask the FDA to allow a generic to certify to a brand name or reference drug no longer on the market or to allow approval of a generic that differs slightly[250] from the brand-name drug in regards to characteristics such as strength or dosage form.[251]

Other petitions, however, are troubling, particularly some of the petitions that assert concerns regarding a generic application or request that the

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[245] *See infra* Section V.D.

[246] CTR. FOR DRUG EVALUATION & RES., *supra* note 196, at 272 (statement by Jane Axelrad, Associate Director of Policy, Center for Drug Evaluation and Research) (discussing difficulties of getting parties to work together to set up a joint REMS). At least one bill has been introduced in Congress tackling the two main forms of REMS abuse—denial of samples for generic testing, and unwillingness to cooperate on single-shared REMS. The bill would require brand-name drug companies to provide samples (after FDA approval) to prospective generics at a nondiscriminatory, commercially reasonable, market-based price. It would also streamline the process by which ANDA applicants can receive a waiver from the single-shared REMS process if they are able to demonstrate that negotiations were not successful after 120 days. *See* Fair Access for Safe and Timely Generics Act of 2015, H.R. 2841, 114th Cong. (2015).

[247] Federal Defendants' Opposition to Plaintiff's Motion for a Temporary Restraining Order And/Or Preliminary Injunction, Prometheus Lab. Inc. v. Burwell, No. 15-cv-00742, at 15 (D.D.C. May 28, 2015), http://www.fdalawblog.net/LOTRONEX%20-%20Roxane%20TRO-PI%20Opp.pdf [https://perma.cc/LZ5U-WGZ4].

[248] 21 C.F.R. § 10.30 (1979).

[249] Hyman, Phelps & McNamara PC, *FDA Citizen Petition Tracker*, FDA LAW BLOG (Feb. 29, 2016), www.fdalawblog.net/fda_law_blog_hyman_phelps/files/CPTracker.xls [https://perma.cc/J4LD-G88R].

[250] These are known as "ANDA suitability petitions." Kurt R. Karst, *FDA Rejects Requests to Initiate Rulemaking for (505)(b)(2) NDA Therapeutic Equivalence Rating Decisions*, FDA LAW BLOG (July 28, 2014), http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2014/07/fda-rejects-requests-to-initiate-rulemaking-for-505b2-nda-therapeutic-equivalence-rating-decisions.html [https://perma.cc/T8CR-89QS].

[251] *See id.*

generic applicant conduct new, time-consuming studies before approval.[252] As described previously, even if a petition costs hundreds of thousands of dollars to file, the investment could pay off. The value of the delay could be lucrative, even when the petition is quickly rejected.

Suboxone, the case that featured creative product hopping and allegations of REMS abuse, again provides a troubling tale. As described in the previous section, the generics were forced to get a REMS waiver because they were unable to get the brand-name company, Reckitt, to cooperate. Immediately prior to the generic REMS waiver request, which would have allowed the generic to move forward if and when approved, Reckitt announced that it was completely pulling Suboxone tablets from the market (but did not immediately do so).[253] The company cited safety concerns related to pediatric exposure, and it followed up on the same day with a citizen petition asking the FDA to refrain from approving any generic application for Suboxone.[254] In its citizen petition, the brand-name company again cited pediatric exposure issues to demand that medications—such as generic Suboxone—come with "targeted educational interventions on the risk of pediatric exposure" and unit-dose packaging.[255]

The FDA has a process that allows an application to move forward for a generic version of a drug no longer on the market, if the FDA determines that the drug was not removed for safety reasons.[256] The safety move coupled with the citizen petition may have been intended to block the generic from utilizing this pathway.

Complainants in *In re Suboxone* allege that this citizen petition was a sham merely meant to block generic approval.[257] Specifically, the requested labeling measures for generic Suboxone were never required for the brand-name Suboxone tablets. In addition, the FDA does not have the ability to require that a generic filer add labeling not approved for the brand-name drug.[258] Most important, Reckitt continued to sell Suboxone tablets in bulk and without unit-dose packaging even after it made the petition requesting these restrictions for the generic version.[259]

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[252] Carrier & Wander, *supra* note 141, at 261.

[253] *In re* Suboxone (Buprenorphine Hydrochloride and Naloxone) Antitrust Litig., 64 F. Supp. 3d 665, 675–76 (E.D. Pa. 2014).

[254] *Id.*; *see* Citizen Petition from Reckitt Benckiser Pharm., Inc. to Div. of Dockets Mgmt., U.S. Food and Drug Admin. (Sept. 5, 2012) [hereinafter Citizen Petition from Reckitt Benckiser], https://www.naabt.org/documents/Reckitt_Benckiser_Pharmaceuticals_Inc_2012_FDA_Citizen_Petition.pdf [https://perma.cc/G4Z3-BFTA].

[255] *Id.*

[256] 21 C.F.R. § 314.161 (2015). A generic can file a citizen petition asking for an official determination of whether the reference drug was "withdrawn for safety or effectiveness reasons." If it is determined that the drug was not withdrawn for those reasons, the drug will be relisted for the purposes of ANDA submissions.

[257] *In re Suboxone*, 64 F. Supp. 3d at 676.

[258] *Id.*

[259] *Id.* at 676–77.

The FDA denied the brand-name company's citizen petition and immediately thereafter granted approval for two generic versions of Suboxone tablets.[260] In its denial of the petition, the FDA noted that the brand-name company's "own actions . . . undermine, to some extent, its claims with respect to the severity of this safety issue."[261] Further, the FDA noted that the brand-name company's decision to pull Suboxone from the market so close to generic competition "cannot be ignored," explaining in a footnote that Reckitt got access to private information about the potential timing for generic applications because the generics volunteered this information in an attempt to get the company to cooperate in REMS creation.[262] The FDA explicitly said it was not denying the petition for failing to raise a valid scientific or regulatory issue or for purposeful obstruction of a generic application, preferring to focus on the lack of merits of the petition's safety concerns. The Agency, nevertheless, made its opprobrium clear by referring the company's conduct to the Federal Trade Commission for review.[263] Still, despite the FDA's complete rebuttal of all of the brand-name company's claims, the citizen petition resulted in five months of delay. Given sales of approximately $1.5 billion in 2012, the five months of delay was worth over $600 million in unchallenged sales to the brand-name company.[264] That is a remarkably strong incentive for companies to engage in this type of tactic. As always, the consumer pays the cost in the form of higher prices.

The FDA and the Federal Trade Commission have long recognized that the citizen petition process could be subject to abuse, expressing concerns and proposing modifications as early as 1999.[265] Congress attempted to curb

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[260] *Id.* at 676.

[261] Letter from Janet Woodcock, Dir., Ctr. for Drug Evaluation & Research, to Tim Baxter, Glob. Medical Dir., Reckitt Benckiser Pharm., Inc., No. FDA-2012-P-1028, at 15 (Feb. 22, 2013) [hereinafter FDA Response to Reckitt Benckiser], http://www.regulations.gov/#!documentDetail;D=FDA-2012-P-1028-0011 [https://perma.cc/3UGE-BQLN]; Letter from Robert L. West, Deputy Dir., Office of Generic Drugs, U.S. Food & Drug Admin., to Janak Jadeja, Dir., Regulatory Affairs, Actavis Elizabeth LLC (Feb. 22, 2013), http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2013/091422Orig1s000ltr.pdf [https://perma.cc/9EZB-F3C3] (approving generic Suboxone tablets on the same day the citizen petition was denied); Letter from Robert L. West, Deputy Dir., Office of Generic Drugs, U.S. Food & Drug Admin., to Candice Edwards, Senior Vice President, Regulatory & Clinical Affairs, Amneal Pharm. (Feb. 22, 2013), http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2013/203136Orig1s000ltr.pdf [https://perma.cc/4GE4-VDUE] (approving generic Suboxone tablets on the same day the citizen petition was denied).

[262] FDA Response to Reckitt Benckiser, *supra* note 261, at 15 & n.53.

[263] FDA Response to Reckitt Benckiser, *supra* note 261, at 16. FTC proceedings are now underway against Reckitt Benckiser. *See* FTC v. Reckitt Benckiser Pharm., Inc., No. 14-MC-005, 2014 WL 4792175 (E.D. Va. Sept. 24, 2014) (court proceedings over release of documents for the FTC's investigation).

[264] *Suboxone Sales Data*, DRUGS.COM (Feb. 2014), http://www.drugs.com/stats/suboxone [https://perma.cc/23F5-W3D6]. As with all calculations of the value of delay in this Article, the assumption is made for ease that, without the delay, generic competition would immediately drop Reckitt's revenues on Suboxone to zero.

[265] *See* Darren S. Tucker, *FDA Citizen Petition: A New Means of Delaying Generic Entry?*, 20 ANTITRUST HEALTH CARE CHRON. 10, 11 (2006); Citizen Petitions; Actions That Can be Requested by Petition; Denials, Withdrawals, and Referrals for Other Administrative Ac-

such abuse by enacting a new rule in 2007 that when a citizen petition could delay generic approval, the FDA must take final action on the petition within 150 days, unless the delay is necessary to protect the public health.[266] To further discourage baseless or strategically-timed petitions, filers of citizen petitions must provide the date when they first became aware of the issues raised.[267] Finally, the FDA also was granted the power to deny a petition at any time if it believes a petition was "submitted with the primary purpose of delaying the approval of an application and the petition does not on its face raise valid scientific or regulatory issues."[268]

In the case of *Suboxone*, however, the regulatory process worked entirely as intended, and the brand-name company's petition was denied exactly 150 days after the date it was filed. Nevertheless, the petition resulted in five months of delay and an estimated $600 million of higher priced sales for the company.[269] Thus, even when the bell rings on time as Congress intended, brand-name companies still can use the process to engage in costly delays. The various amendments also do not seem to have discouraged the filing of non-meritorious citizen petitions requesting the delay of a generic. Between fiscal years 2008 and 2013—the period in which the amendments have been in place—124 delay petitions were filed and only eight were fully

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tion, 64 Fed. Reg. 66822-01 (proposed Nov. 30, 1999) (to be codified at 21 C.F.R. pt. 10) (withdrawn); Fed. Trade Comm'n, Comment Letter on Citizen Petition; Actions That Can be Requested by Petition; Denials, Withdrawals, and Referrals for Other Administrative Action (Mar. 2, 2000), https://www.ftc.gov/sites/default/files/documents/advocacy_documents/ftc-staff-comment-food-and-drug-administration-concerning-citizen-petitions/v000005.pdf [https://perma.cc/F8DF-24BF].

[266] Codified at 21 U.S.C. § 355(q) (2012), *amended by* Improving Regulatory Transparency For New Medical Therapies Act, Pub. L. No. 114-89, 129 Stat. 698 (2015). The dead- line was originally set as 180 days—the Food and Drug Administration Safety and Innovation Act ("FDASIA"), passed in 2012, shortened the approval period to 150 days. 21 U.S.C. § 355(q)(2)(A) (2012) (establishing the 150-day deadline for agency action); 21 U.S.C. § 355(q)(1)(A)(ii) (2012) (establishing the public health exception); *see also* Kurt R. Karst, *The Coming 505(q) Citizen Petition Cliff and Some Interesting Petition Strategies*, FDA LAW BLOG (Sept. 4, 2012), http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2012/09/the- coming-505q-citizen-petition-cliff-and-some-interesting-petition-strategies.html [https://perma.cc/VQG9-MTD7] (presenting more details about the 2007 and FDASIA changes).

[267] 21 U.S.C. § 355(q)(1)(H)(c) (2012).

[268] 21 U.S.C. § 355(q)(1)(E) (2012).

[269] *See Suboxone Sales Data*, *supra* note 264 (listing Suboxone sales as $1.5 billion in 2012, or $600 million over five months).

granted.[270] Moreover, the number of citizens petitions requesting delay has not declined since passage of the amendments.[271]

The amendment's most biting provision also has proven difficult to apply. Recall that the statute allows the FDA to summarily deny petitions, but only when they are both submitted for the main purpose of delay and raise no valid scientific or regulatory issues on their face. Proving both of these requirements concurrently has turned out to be quite difficult. In fact, since the amendments took effect in fiscal year 2008, the FDA has never applied the summary denial provision.[272]

In theory, the wounded would-be generic could file a lawsuit asserting that the brand-name company engaged in anticompetitive behavior by submitting a sham citizen's petition. Such a lawsuit is unlikely to succeed, however.[273] The difficulty flows back to *Noerr-Pennington*, a line of Supreme Court cases from the 1960s that establishes a general right to petition the government without fear of antitrust liability.[274] *Noerr-Pennington* does carve out an exception that allows antitrust liability when petitioning the government is a sham meant merely to interfere with a competitor.[275] The Court, however, has set an extremely high standard for demonstrating that a legal petition is a sham. Specifically, the petition must be objectively baseless, which requires a showing that no reasonable petitioner can realistically expect success on the merits, as well as subjectively baseless, which requires a showing that the petition tries to conceal an attempt to interfere directly

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[270] U.S. FOOD & DRUG ADMIN., SIXTH ANNUAL REPORT TO CONGRESS ON DELAYS IN APPROVALS OF APPLICATIONS RELATED TO CITIZEN PETITIONS AND PETITIONS FOR STAY OF AGENCY ACTION FOR FISCAL YEAR 2013, at 6–7 (2013) [hereinafter FDA SIXTH ANNUAL REPORT FOR FY 2013], http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ReportsBudgets/UCM423291.pdf [https://perma.cc/L4EF-2CP3]. Thirty-one of these petitions were denied in part or granted in part. *Id.* at 6. However, as Carrier notes, these "mixed decisions" are often a formality and not truly a partial finding in favor of the petitioner. The requests "granted in part" are often trivial re- quests for bioequivalence studies that have either already been completed, are in progress, or would certainly be required by the FDA even in the absence of the citizen petition. Carrier & Wander, *supra* note 141, at 266–68.

[271] FDA SIXTH ANNUAL REPORT FOR FY 2013, *supra* note 270, at 5; *see generally* Carrier & Wander, *supra* note 141.

[272] FDA SIXTH ANNUAL REPORT FOR FY 2013, *supra* note 270, at 7. *See generally* Seth C. Silber, Jonathan Lutinski & Rachel Taylon, *Abuse of the FDA Citizen Petition Process: Ripe for Antitrust Challenge?*, 25 ANTITRUST HEALTH CARE CHRON. 26 (2012).

[273] *See* Silber, Lutinski & Taylor, *supra* note 272, at 30.

[274] For a detailed description of the development of *Noerr-Pennington*, see generally Robin Feldman, *Federalism, First Amendment, & Patents: The Fraud Fallacy*, 17 COLUM. SCI. & TECH. L. REV. 30 (2015).

[275] United Mine Workers v. Pennington, 381 U.S. 657, 669–72 (1965); E. R.R. Presidents Conf. v. Noerr Motor Freight, Inc., 365 U.S. 127, 144 (1961); *see also* Silber, Lutinski & Taylon, *supra* note 272, at 30; FELDMAN, *supra* note 13, at 166; Robin Feldman, *Intellectual Property Wrongs*, 18 STAN. J.L. BUS. & FIN. 250, 301–05 (2013) (suggesting that there may be a pathway for proving sham litigation, at least with actions that demonstrate multiplicity).

with competition through the administrative process.[276] This burden on plaintiffs is crushing.

Still other pathways exist for abusing the citizen petition process, despite the limitations imposed by the amendments. As the FDA itself has noted, the 150-day clock applies only when a citizen petition has the power to delay generic approval.[277] If a citizen petition is filed before any generic application is submitted or before any generic application is ready for approval under the Hatch-Waxman rules, the 150-day deadline does not apply.[278] Thus, citizen petitions filed before a generic application is ready can serve as yet another obstacle, perhaps combined with strategies already in play.

Finally, the 150-day limit applies to consideration of each petition, rather than providing a 150-day maximum for how long generic approval can be put on hold. That leaves the door open for what the FDA has called "serial" petitions, in which multiple petitions are filed about the same drug, frequently from the same petitioner.[279] By filing separate petitions at staggered times on disparate issues, a brand-name company can force the FDA to spend time responding to each petition, thereby potentially lengthening the total delay-by-citizen-petition far beyond 150 days.[280] Thus, as with REMS delay, codified congressional condemnations of a practice[281] are just a new rule for which manufacturers must find a work-around. They are about as effective as admonishing school children to speak politely to each other on the playground.

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[276] Professional Real Estate Inv'rs. v. Columbia Pictures Indus., 508 U.S. 49, 60–61 (1993); *see also* Silber, Lutinski & Taylon, *supra* note 272, at 30–31; FELDMAN, *supra* note 13, at 166–67.

[277] FDA SIXTH ANNUAL REPORT FOR FY 2013, *supra* note 270, at 6.

[278] WILSON SONSINI GOODRICH & ROSATI, CITIZEN PETITIONS AIMED AT DELAYING GENERIC COMPETITION REMAIN A CONCERN 1 (2015), https://www.wsgr.com/publications/PDF-Search/wsgralert-citizen-petitions.pdf [https://perma.cc/HA6X-FJ67]; *see also* FDA SIXTH ANNUAL REPORT FOR FY 2013, *supra* note 270, at 6.

[279] FDA SIXTH ANNUAL REPORT FOR FY 2013, *supra* note 270, at 7.

[280] *Id.*; WILSON SONSINI GOODRICH & ROSATI, *supra* note 278, at 2. In the FDA's Fourth Annual Report on delays related to citizen petitions for the 2011 fiscal year, it noted the following about serial petitioning: "[F]or example, the agency received its fourth 505(q) petition relating to the approval of ANDAs for topical ophthalmic products and a third 505(q) petition related to Doryx (doxycycline). The various submissions raised different scientific issues, requiring serial review of different arguments, rather than one comprehensive review of all pertinent arguments." U.S. FOOD & DRUG ADMIN., FOURTH ANNUAL REPORT TO CONGRESS ON DELAYS IN APPROVALS OF APPLICATIONS RELATED TO CITIZEN PETITIONS AND PETITIONS FOR STAY OF AGENCY ACTION FOR FISCAL YEAR 2011, at 6 (2011), http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ReportsBudgets/UCM369782.pdf [https://perma.cc/MZ7V-DEZG].

[281] Referring to the REMS statute passed by Congress clarifying that a REMS cannot be used to block an ANDA and Section 505(q) for citizen petitions.

E. Preventing the "Skinny Label": Blocking Section viii Carve-Outs

As Generation 3.0 games advance, an additional tactic relates to what is known as "the skinny label." Many patents on pharmaceuticals do not cover substances and chemical formulas, but particular uses of a drug. Hatch-Waxman, however, allows a generic applicant to seek approval for a version that will cover only uses of the drug not protected by patents or FDA exclusivities.[282] Applicants also can ask permission to omit some of the brand-name drug's labeling language from the generic label if that language relates to uses that are protected.[283] These are known as section viii carve-outs or "skinny labels." For example, the brand-name company's patent could be a "method-of-use" patent, which protects only certain indications of the drug, with "indication" referring to a reason why the drug is administered (e.g. "for treatment of *Helicobacter* infections").[284] This could occur when the drug's chemical formula had been patented or used in the past, and the company could receive only a more limited patent for a new indication of the medicine. Under these circumstances, the generic could request approval for uses of the medication other than those protected by the use patent.

Request for a "skinny label" could also apply when the brand-name drug company has received special FDA exclusivities available for circumstances such as use of a drug for orphan categories or new pediatric indications. A generic could file a request indicating that it does not seek approval for the protected uses. Similarly, if a brand-name drug is only protected by non-indicatory patents or FDA exclusivities for reasons such as how the drug should be administered or its bioavailability under certain conditions, a generic applicant could state that their drug would not be subject to the protected labeling.[285]

Generally, these carve-out requests are approved unless they cause the generic to be less safe or effective than the brand-name drug for all remaining, non-protected uses.[286] Such carve-outs or "skinny labels" can be an effective way for generics to bypass weak or limited patents that brand-name companies may add near the end of a drug's patent term in the hopes of holding onto its exclusive market position for all uses of a drug.

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[282] 21 U.S.C. § 355(j)(2)(A)(viii) (2012).

[283] 21 C.F.R. § 314.127 (2015).

[284] The example indication of "use for treatment of *Helicobacter* infections" comes from the FDA's listed use code for a method-of-use patent listed for Nexium, the popular acid reflux medication—although this use refers to using Nexium to treat bacterial infections often associated with stomach ulcers and cancer. *See* Patent and Exclusivity Search Results from *Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations*, U.S. FOOD & DRUG ADMIN., http://www.accessdata.fda.gov/scripts/cder/ob/docs/patexclnew.cfm?Appl_No=021153&Product_No=002&table1=OB_Rx [https://perma.cc/TJ9B-HUWL] (last updated Feb. 2016) (patent no. 8,466,175 at the bottom of the list); U.S. Patent No. 8,466,175 (filed Nov. 17, 2011). The patent was filed more than ten years after Nexium first received FDA approval.

[285] 21 C.F.R. § 314.127 (2015).

[286] *Id.*

For every action, however, there is an equal and opposite reaction, and that is certainly the case for carve-outs. Under Hatch-Waxman, when a generic application requests only section viii carve-outs (but contains no Paragraph IV certifications), that application does not trigger the artificial act of patent infringement that allows for litigation and a 30-month stay on approval. Thus, the generic application should be eligible for immediate approval.[287] Undaunted, brand-name companies file citizen petitions, arguing that the carve out should be disallowed. These petitions generally argue that the requested carve-out contains information related to the safety or efficacy of the drug, and that such information cannot be removed from the label.[288] A generic could, indeed, be attempting disingenuously to get around the Hatch-Waxman litigation process by removing certain uses from the label knowing that physicians may prescribe the drug for all uses, nonetheless.[289] The off-label use of medication is a widespread phenomenon that affects many aspects of pharmaceutical law.[290] Nevertheless, there are clear instances of brand-name companies making small labeling changes or securing

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[287] Lisa Barons Pensabene & Dennis Gregory (on behalf of Fitzpatrick, Cella, Harper, and Scinto), *Hatch-Waxman Act: Overview*, PRACTICAL L. CO. 4 (2013), http://www.fitzpatrickcella.com/DB6EDC/assets/files/News/Hatch-Waxman%20Act%20Overview%20lpensabene_dgregory.pdf [https://perma.cc/KU8C-ELG8]. There are also scenarios where an ANDA filer uses a Paragraph III or IV certification for some patents and carves out other patents via a section viii statement.

[288] *See, e.g.*, Citizen Petition from Ernest Lengle, Exec. Dir. Regulatory Affairs, Watson Labs., Inc., to Div. of Dockets Mgmt., U.S. Food & Drug Admin., No. FDA-2008-P-0069- 0001, at 2 (Jan. 29, 2008), http://www.regulations.gov/#!documentDetail;D=FDA-2008-P- 0069-0001 [https://perma.cc/88J5-W822] (requesting that the FDA refrain from allowing a carve-out for irinotecan hydrochloride on grounds that it would render the generic less safe or effective than the listed drug).

[289] Brand-name drug companies have expressed concern that carve-outs only remove uses and indications in name only—once on the market, the generics could be prescribed and used "off-label" for all uses approved for the brand-name version. *See* Citizen Petition from Robert Church & David Fox, Hogan Lovells US LLP on behalf of Spectrum Pharmaceuticals, Inc., to Div. of Dockets Mgmt., U.S. Food & Drug Admin., No. FDA-2014-P-1649, at 12 (Sept. 30, 2014), http://www.regulations.gov/#!documentDetail;D=FDA-2014-P-1649-0001 [https://perma.cc/8RWM-YQ5N]. However, the FDA has refused to accept this as a rationale for not approving a carve-out, even in cases where the reference listed drug holder says off-label use could implicate safe and effective use of the drug. *See* Letter from Janet Woodcock, Dir., Ctr. for Drug Evaluation & Research, to Robert Church & David Fox, Hogan Lovells US LLP, No. FDA-2014-P-1649, at 13–14 (Feb. 24, 2015), http://www.regulations.gov/#!documentDetail;D=FDA-2014-P-1649-0005 [https://perma.cc/L5Q9-A6MY]. The FDA said requiring this type of "foreseeable use" analysis is "inconsistent with our long-standing policy of not interfering with the practice of medicine," and noted that a circuit court already rejected this argument as a bar to generic approval. *See id.* at 14 n.27 (citing Sigma-Tau Pharm., Inc. v. Schwetz, 288 F.3d 141 (4th Cir. 2002)).

[290] For example, pharmaceutical companies have enjoyed considerable success in recent years in convincing courts that FDA restrictions on truthful statements about off-label uses of drugs may violate free speech. *See generally* United States v. Caronia, 703 F.3d. 149 (2d Cir. 2012); Amarin Pharm., Inc. v. U.S. Food & Drug Admin., 119 F. Supp. 3d 196 (S.D.N.Y. 2015). For a discussion of the widespread off-label uses of drugs, see *Amarin*, 119 F. Supp. 3d at 200–01.

weak method-of-use patents and then filing citizen petitions to block the carve-out requests that follow.[291]

The history of Skelaxin, while complicated, is one of the most demonstrative in this area, showing how adding one or two method-of-use patents along with clever labeling can lead to years of delay. Skelaxin, the brand-name for the well-known muscle relaxant metaxalone, was first approved back in 1962.[292] The drug did not face the threat of generic competition for over thirty years, even though the initial patent on the active ingredient expired in 1979.[293] The competitive landscape changed, however, in 2001, when a company filed for approval to market generic Skelaxin.[294]

With generic competition on the horizon, the brand-name drug company went to work on extending the monopoly market for the drug. In 2001, the company conducted a study measuring the bioavailability when Skelaxin is taken on a full stomach compared to its bioavailability in a fasting state.[295] The study showed that the bioavailability of Skelaxin increases when taken with food—in particular, a "high fat meal."[296] Next, the brand-name company filed for and received two patents in 2002 on the method of "increasing the bioavailability of metaxalone" by taking it with food.[297] In June 2002, the FDA approved a labeling amendment for Skelaxin, adding a

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[291] Brand-name companies also have sought to block carve-outs by modifying the "use codes" associated with a given patent in the Orange Book. Use codes provide a brief description of what use of the drug is covered by the listed patent, and brand-name companies have been accused of trying to broaden the scope of use codes to prevent a section viii carve-out. Like the patents listed in the Orange Book, use code information is not verified by the FDA. In *Caraco v. Novo Nordisk*, 132 S. Ct. 1670 (2012), however, the Supreme Court found that generic manufacturers can file a statutory counterclaim seeking correction of an inaccurate use code.

[292] *FDA Approved Drug Products*, U.S. FOOD & DRUG ADMIN., http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.Label_ApprovalHistory#apphist [https://perma.cc/5BNH-Q9L6] (enter drug name [Skelaxin] in search bar and click "submit.").

[293] Consolidated Class Action Complaint and Jury Demand at 10, United Food & Commercial Workers Union & Midwest Health Benefits Fund v. King Pharm., Inc., No. 12-cv- 00085 (E.D. Tenn. Mar. 8, 2012), ECF No. 1, *consolidated into* Skelaxin (Metaxalone) Anti- trust Litig., No. 12-md-02343 (E.D. Tenn. June 14, 2012), *class certification denied* 299 F.R.D. 555 (2014).

[294] CTR. FOR DRUG EVALUATION & RESEARCH, U.S. FOOD & DRUG ADMIN., APPLICATION NO. ANDA 40-445, APPROVAL PACKAGE FOR ABBREVIATED NEW DRUG APPLICATION APPROVAL 211 (Mar. 31, 2010) [hereinafter ANDA 40-455 APPROVAL PACKAGE], http://www.accessdata.fda.gov/drugsatfda_docs/anda/2010/040445Orig1s000.pdf [https://perma.cc/QPJ4-CE7E] (indicating, in the "Factual Background" of a 2010 Memorandum from Martin Shimer to the Dep't of Heath & Human Servs., that ANDA 040445 was submitted on September 5, 2001). Although all relevant patents had expired at the time of filing, the generic did not receive immediate approval because of chemistry and bioequivalence problems that caused at least two years of delay before the relevant saga begins. *Id.*

[295] Letter from Gary J. Buehler, Dir., Office of Generic Drugs, to Applicant, King Pharm. Inc., at 3 (Mar. 9, 2004) [hereinafter Dear Applicant Letter from Gary J. Buehler], http://www.fda.gov/ohrms/dockets/dailys/04/mar04/031904/04p-0140-cp00001-07-Tab-06-vol1.pdf [https://perma.cc/BH3T-BZJR].

[296] *Id.*

[297] U.S. Patent No. 6,407,128 (filed Dec. 3, 2001); U.S. Patent No. 6,683,102 (filed Mar. 25, 2002).

"pharmacokinetics" section to the drug's labeling with information about the food effect study.[298] With two new patents acquired with expiration dates in 2021, the brand-name company seemed primed to hold on to the Skelaxin market for at least a few additional years.[299]

Now facing two method-of-use patents blocking generic approval, the generic company filed a citizen petition with the FDA in January 2003 asking the agency to restore the previous labeling without the bioavailability data or at least make a declaration that the old label was not withdrawn for safety or effectiveness concerns.[300] In essence, the generic was asking whether this labeling information would be eligible for a labeling carve-out. While not approving the generic company's citizen petition, the FDA filed a "Dear Applicant" letter in 2004, confirming that the bioavailability information could be carved out of generic labeling.[301]

This was a novel case for the FDA, because Skelaxin has only one indication—"relief of discomforts associated with . . . musculoskeletal conditions."[302] Thus, the generic company was not asking to simply carve out a patent-protected use; it was instead seeking to remove labeling information.[303] The FDA ruled, nevertheless, that removing the data would not render generic Skelaxin less safe or effective than the brand-name drug.[304] In rendering its decision, the FDA relied on the fact that the study did not result in any changes to the dosing instructions or the warnings and precautions in the label.[305] The agency also noted that the brand-name company's label specifically states that, "[t]he clinical relevance of these effects is unknown," thus implicating no issues of safe use.[306] With the "Dear Applicant" letter in hand, the generic appeared to have a clear path to a successful carve-out.

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[298] Letter from Lawrence Goldkind, Deputy Dir., Div. of Anti-Inflammatory, Analgesic, & Ophthalmic Drug Prods., U.S. Food & Drug Admin., to Linda B. Fischer, Dir. Regulatory Affairs, Elan Pharm., Inc. (June 20, 2002), http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2002/13217s044ltr_2.pdf [https://perma.cc/5LRG-A2JX] (approving new labeling); *see also* U.S. FOOD & DRUG ADMIN., APPROVED LABEL FOR SKELAXIN (2002), http://www.accessdata.fda.gov/drugsatfda_docs/label/2002/13217s036lbl.pdf [https://perma.cc/PDU9-6YX6].

[299] In 2004, the brand-name drug company complicated matters by withdrawing the 400mg form of Skelaxin and replacing it with a newly-approved 800mg version. While an- other way in which generic competition was frustrated, it is outside of the scope of this current discussion (and, as discussed below, eventually became moot in the generic approval discussion).

[300] ANDA 40-455 APPROVAL PACKAGE, *supra* note 294, at 213 (indicating in row 3 of the table in "Factual Background" of a 2010 Memorandum from Martin Shimer to the Dep't of Heath & Human Servs. that there was a citizen petition in January 2003 requesting that the original label of Skelaxin be restored).

[301] Dear Applicant Letter from Gary J. Buehler, *supra* note 295, at 1.

[302] *Id.* at 1.

[303] *Id.* at 3.

[304] *Id.* at 1–5.

[305] *Id.* at 3.

[306] *Id.* at 3. A footnote appended to this argument in the Dear Applicant letter said that the brand-name drug company's argument might have had more merit had the company conducted clinical trials demonstrating a clinical effect from the differences in bioavailability. *Id.* at 3 n.3.

Immediately thereafter, however, the brand-name company submitted multiple citizen petitions challenging the contents of the FDA's "Dear Applicant" letter.[307] At this point, instead of wading into a new battle over sec- tion viii carve-outs, the generic applicant filed Paragraph IV certifications for the two new patents in late 2004, triggering litigation with the brand-name company.[308] While the lawsuit was underway, the brand-name company worked to strengthen its labeling position, receiving approval for a new label in 2006 which removed the sentence about unknown clinical relevance and added the following sentence to the *Precautions* section of the label: "Taking SKELAXIN with food may enhance general [central nervous sys- tem] depression; elderly patients may be especially susceptible to this CNS effect."[309] Now, the brand-name company had a label with a patent-protected precaution implicating safe use for a drug with only one indication, posing a difficult problem for the generic and the FDA. As the FDA admitted, "[c]arving out patent-protected language from the Precautions section of a label that pertains to a labeled use would generally not be permitted."[310]

The FDA, at an impasse, essentially chose to punt on the issue, making no decision on the brand-name company's citizen petitions. Instead, closure eventually came from the courts five years later, when a Brooklyn-based district court judge invalidated the two bioavailability patents.[311] The judge held that, given what was already known about the drug, it was obvious that Skelaxin would be better absorbed if taken with food.[312] Thus, the generic won its Paragraph IV challenge, and the FDA approved the generic application in 2010, making the carve-out discussion entirely moot.[313]

The delay earned by the brand-name company, however, was not a moot point. From the date that the FDA accepted the first generic application to the date of approval, the brand-name company's tactics delayed the entry of generic Skelaxin for almost a decade, despite the fact that the company lost. The delay may have been worth as much as $3 billion in sales[314]—all

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[307] ANDA 40-455 APPROVAL PACKAGE, *supra* note 294, at 213; *see, e.g.*, Citizen Petition from Peter Mathers, Stacy Ehrlich & Jennifer Davidson, Kleinfeld, Kaplan and Becker, LLP on behalf of King Pharm., Inc. to Div. of Dockets Mgmt., U.S. Food & Drug Admin. (Mar. 18, 2004), http://www.fda.gov/ohrms/dockets/dailys/04/mar04/031904/04p-0140-cp00001-01-vol1.pdf [http://perma.cc/2DGT-WFXD].

[308] ANDA 40-455 APPROVAL PACKAGE, *supra* note 294, at 212.

[309] U.S. FOOD & DRUG ADMIN., APPROVED LABEL FOR SKELAXIN (2006), http://www.accessdata.fda.gov/drugsatfda_docs/label/2006/013217s046lbl.pdf [https://perma.cc/Y8BQ-9H8K] (including the new sentence in the precautions section); *see also* Letter from Bob Rappaport, Div. of Anesthesia, Analgesia & Rheumatology, U.S. Food & Drug Admin., to Douglas Dewar, Senior Dir., Regulatory Affairs, King Pharm., Inc. (Nov. 4, 2006), http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2006/013217s046ltr.pdf [https://perma.cc/RDZ7-PZ59] (noting that the only label change was to the pharmacokinetics information).

[310] ANDA 40-455 APPROVAL PACKAGE, *supra* note 294, at 217.

[311] King Pharm., Inc. et al. v. Eon Labs, Inc., 593 F. Supp. 2d 501 (E.D.N.Y. 2009).

[312] *See id.*

[313] ANDA 40-455 APPROVAL PACKAGE, *supra* note 294, at 227.

[314] The figure of $3 billion was calculated as follows: First, 2002 sales figures of $238 million and 2009 sales of $476 million for Skelaxin were averaged to produce an estimate of

over one sentence on a label and two patents claiming the supposedly novel finding that Skelaxin is better absorbed when taken with food.

IV. Conclusion: Earning a Better Grade for Hatch-Waxman

Thirty years of the Hatch-Waxman regime have brought an extraordinary revolution in the introduction of generic drugs. The progress, however, has not been without resistance. As described above, pharmaceutical companies have engaged in three waves of behaviors to stave off generic competition as long as possible. . . . Generation 3.0 games no longer focus on colluding with generic competitors; instead, the games rely on micro-obstructions against generic companies. These include using administrative processes, regulatory schemes with connections to Hatch-Waxman, and drug modifications to obstruct generics from getting to market. Further, they often combine a number of these tactics to create a multiplicity effect. Micro-obstructions are devilishly difficult to detect and deter. Of course, Generations 3.0 and 2.0 can be combined by developing obstructive behaviors and then promising not to engage in them, using what this article calls boy scout clauses.

Of all of the approaches, the boy scout clauses are perhaps the most cynical. Here, a brand-name company engages in collusive behavior to avoid competition while trying to insulate itself from attack by claiming that it is behaving honorably. While boy scout clauses may be particularly cynical, however, all of the Generation 3.0 approaches threaten a new wave of behaviors that will be difficult for Congress, the courts, and regulatory agencies to control.

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average yearly Skelaxin sales of $357 million. The first full year in which Skelaxin faced a pending ANDA was 2002, while 2009 was the last full year before generic approval. Then, $357 million was multiplied by 9, representing approximately 9 years of delay, to reach a total value of $3.2 billion. Press Release, King Pharm., King Pharmaceuticals Acquires Primary Care Business Unit from Elan (Jan. 30, 2003), http://www.sec.gov/Archives/edgar/data/1047699/000095014403000944/g80411exv99w1.txt [https://perma.cc/5FYD-7VCG] (noting 2002 sales of $238 million); Press Release, Sandoz, Sandoz Announces Launch of First Generic Version of Leading Muscle Relaxant Skelaxin (May 20, 2010), http://www.fiercepharma.com/press-releases/sandoz-announces-launch-first-generic-version-leading-muscle-relaxant-skelaxin-anda-e [https://perma.cc/P5NC-NBZ6] (noting 2009 sales of $476 million).

A. Societal Harms

The strategic behaviors in the Hatch-Waxman arena are troubling from the perspective of the theoretical underpinnings of both patent and antitrust law. The patent concern traces back to the constitutional provision that frames all of patent law. From the activities that should be free to all and reserved to none, the patent system chooses to dedicate to some, for a limited period of time, the exclusive use of an innovation based on the theory that this exclusion will redound to the benefit of society.[315] The bargain, however, is not unlimited. When the patent expires, everyone should be free to engage in those activities, returning to a competitive environment. Hatch- Waxman is intended to ensure the prompt return to a competitive environment at the end of the patent term, as well as to create incentives to weed out weak patent claims that are improperly keeping competitors out of the particular innovative space. Pharmaceutical company behavior that extends the period in which the company can hold off competition runs contrary to the patent bargain.

The behaviors described in this article also raise antitrust concerns, although those concerns are framed at a slightly different angle.[316] As a general matter in antitrust doctrine, big is not bad; it is what you do with your size that matters.[317] Thus, brand-name companies that have earned a monopoly in the market with their blockbuster drugs are targets of antitrust concern only when they attempt to extend their monopoly improperly by colluding with competitors or inappropriately suppressing competition. As scholarly works by this author and others have noted, agreements not to compete and activities that abuse the regulatory process to block competitors raise anti-trust concerns.[318] Thus, when pharmaceutical company behavior improperly delays or impedes the entry of generic competition, that behavior runs contrary to the open, competitive market environment for which antitrust law yearns.

The theoretical concerns translate into tangible damage to society as well. With patents, the legal system chooses to tolerate certain societal losses for the innovation effects that may result. When brand-name companies extend their monopoly power beyond the expiration of the patent, however, there are unanticipated deadweight losses to society in the form of higher prices. Whether Congress has chosen the optimal parameters for the patent

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[315] *See* U.S. CONST., art. I, § 8, cl. 8 ("To promote the Progress of [the] useful Arts, by securing for limited Times to . . . Inventors the exclusive Right to their respective . . . Discoveries."); *see also* Robin Feldman, *Intellectual Property Wrongs*, 18 STAN. J.L. BUS. & FIN. 250, 318 (2013).

[316] For a discussion of the differing perspectives of patent law and antitrust law regarding inappropriate behavior by patent holders, see generally Feldman, *supra* note 67.

[317] Tom Ewing & Robin Feldman, *The Giants Among Us*, 2012 STAN. TECH. L. REV. 1, 26 (2012).

[318] *See, e.g.*, *id.* at 26–33; Carrier, Levidow & Kesselheim, *supra* note 198, at *31; Hemphill, *An Aggregate Approach to Antitrust*, *supra* note 53, at 10.

system is a separate question. Once those parameters are set, behaviors that cause additional deadweight losses for society are contrary to the system's incentive structure, and the damage to society should not be tolerated.

The Hatch-Waxman manipulations also are damaging to society in the form of activities that are wasteful for companies and institutions alike. Hide-and-seek games that the courts, the FDA, the FTC, and the Patent and Trademark Office are forced to play are wasteful to all. The games are particularly burdensome on the court system, with pharmaceutical litigation over generic competition now joining patent troll litigation as a major component of new patent lawsuit filings.[319] Sadly, given the amount of money at stake, the behaviors are likely to continue unless the legal system finds a way to change the incentives or to create sufficient disincentives. This is not to suggest that progress has been negligible. The shift from simple pay-for- delay agreements to side deals and then to micro-obstructions reflects the progress that regulatory agencies have begun to achieve in the courts. In addition, although micro-obstructions can create a valuable delay in competition, they are more difficult to achieve and often less lengthy than pay-for- delay.

Nevertheless, although the form of the behavior may have shifted, the behavior remains. And although changes such as the Supreme Court decision in *Actavis* and various congressional amendments have been important, by the time the changes are implemented, the market has moved beyond. The question is, what should come next.

The following discussion explores new directions for the legal system in its continuing efforts to alleviate the gamesmanship that the Hatch-Wax- man system has wrought. The discussion is not intended to provide a blueprint for legislation or a description of specific doctrinal provisions. Rather, it is an attempt to suggest the contours of how new approaches could be structured, and to generate discussion of a shift in approach.

B. Systems, Simplification, Sunshine, and Standards-Based Doctrines

In addition to the approaches that have been undertaken so far, managing the evolution of the Hatch-Waxman games will require a systems approach. One could use an analogy from the medical field itself.[320] Under the old approach to cancer treatment, physicians would attack a tumor by trying

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[319] *See* Jacqueline Bell, *Smartphone, Pharma Giants Dominate List of Top IP Targets*, LAW360 (Feb. 10, 2016), http://www.law360.com/articles/756254/smartphone-pharma-giants-dominate-list-of-top-ip-targets [https://perma.cc/86LP-PTC6] (noting that the number of new patent lawsuits filed in 2015 increased by fifteen percent over the prior year and that generic pharmaceutical companies were frequent targets of those lawsuits, along with technology companies); *2015 Patent Dispute Report*, UNIFIED PATS. http://unifiedpatents.com/2015-year-end-report/ [https://perma.cc/2BD7-7V2H] (showing the prevalence of lawsuits filed by non-practicing entities in 2015).

[320] This system theory example is taken from Robin Feldman, *Cultural Property and Human Cells*, 21 INT'L J. CULTURAL PROP. 1, 6 (2014).

to reduce its size or deny substances that seemed to be feeding it. Modern medical research has suggested, however, that cancer treatment can be far more effective when using a systems approach. Specifically, tumors seem to operate in a networked or systems fashion. Cutting off one approach may simply lead the tumor to develop work-around approaches, and the new approaches may be even more dangerous and damaging than the original pathway. Thus, attacking the problem by trying to mitigate it when it emerges may be as outdated an approach for the patenting and approval of medicines as it is for treatments in which those medicines will be involved.[321]

Taking a systems approach may allow us to move away from what one of the authors has called death by tinkering—a problem endemic throughout the patent system.[322] In this problematic approach, legal actors address difficult questions by adjusting the doctrines a little here and a little there without developing a comprehensive logic for the full breadth of the legal area. Eventually, the entire doctrinal base threatens to collapse under its own weight.

One can see a classic example of death by tinkering in the Federal Circuit's failed attempts to create a workable rule for determining what types of inventions should qualify as patentable subject matter. For years, the court clung to its "machine-or-transformation" test, making ever finer distinctions to try to avoid uncomfortable results. In the end, the test required considerable hand waving, and one had to suspend a certain amount of disbelief to overlook the logical discrepancies.[323] After a series of three cases gently encouraging the Federal Circuit to develop a workable test, the Supreme Court eventually gave up and supplied its own test.[324]

A similar phenomenon plagues the various doctrines related to whether the definition of an invention reaches beyond the state of the art at the time of the invention. Doctrines developed for mechanical inventions, in which one generally understands all aspects of the technology, have led to uncomfortable results for biologic inventions, in which many unknown factors may

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[321] *Cf.* Robin Feldman, *Intellectual Property Wrongs*, 18 STAN. J.L. BUS. & FIN. 250, 255 (2013) (noting that when a comprehensive problem exists, the answer lies in attacking its roots, in addition to trimming the tendrils as they emerge in various places).

[322] *See* Robin Feldman, *A Conversation on Judicial Decision-Making*, 5 HASTINGS SCI. & TECH. L.J. 1, 2 (2013) (introducing the concept in the context of Federal Circuit attempts to fix problems in patent doctrines such as patentable subject matter without taking into account the doctrinal area as a whole).

[323] *See* Robin Feldman, *Coming of Age for the Federal Circuit*, 18 GREEN BAG 2D 27, 32–33 (2014). For a detailed discussion of the problems with the Federal Circuit's machine-or-transformation test, see Feldman, *supra* note 322, at 15–20, 23–25. *See also* FELDMAN, *supra* note 13, at 113–24 (describing various failed tests the Federal Circuit has tried for patentable subject matter).

[324] Feldman, *Coming of Age*, *supra* note 323, at 7 (describing the final opinion in the Supreme Court's quartet, *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 134 S. Ct. 2347 (2014), along with the Justices' three prior attempts to prompt the Federal Circuit in *Bilski v. Kappos*, 561 U.S. 593, 659 (2010), *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 132 S. Ct. 1289 (2012), and *Association for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107 (2013)).

be at play. For example, when an invention is a doorknob, one generally understands the various parts and their operation. There are no unexplained pieces and no hints that the door frame may be integrating with the door in ways no one has dreamed.[325] Such is not the case with biotechnology inventions, however, and in that realm, society grants rights in the face of significant unknowns.

Doctrinal rules that fit comfortably with mechanical inventions can lead to uncomfortable results in life science cases. Struggling with the problem, different Federal Circuit panels have created doctrinal rules that contradict each other and point in different theoretical directions.[326] The rules reach what seem to be good results in each case, but at the expense of doctrinal coherence and the ability to predict the boundaries of patents going forward. The entire area now threatens to collapse. Doctrines related to defining an invention for purposes of comparing it to later inventions are clashing against doctrines related to defining the invention for purposes of comparing it to earlier inventions. Unless one is happy holding up a piece of fruit and declaring that looking in one direction, it is an apple, and looking in another direction, it is an orange, the doctrines are untenable.[327]

Therefore, the first step in a systems approach would involve focusing on the extent to which different systems interact in the process. These include not only the patent approval system, but also the patent litigation sys- tem,[328] FDA approval systems—including the Orange Book, REMS, citizens petitions, and other FDA processes—and antitrust doctrines as they may apply to this arena. Effective progress will require working with all of these systems at the same time, lest adjustments to one area lead to counteraction in another. With thirty years of Hatch-Waxman experience, it is time to consider a comprehensive overhaul of the system for generic approval, one that looks more broadly at the interaction of all of the systems.

The second step is to ruthlessly simplify. For those who value complexity, the Hatch-Waxman system is a garden of delights. Complexity breeds opportunity, however, and, in the case of Hatch-Waxman, the Act's complexity has spawned opportunities for manipulation. An overhaul of the Hatch-Waxman system that resulted in equivalent or even greater complexity would serve little purpose, other than as a full employment act for lawyers. In contrast, a simplified, slimmed-down system would provide fewer opportunities for clever gamesmanship, as well as absorbing fewer resources for the system as a whole.

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[325] The doorknob example is described more fully in Robin Feldman, *Rethinking Rights in Biospace*, 79 So. Cal. L. Rev. 1, 8–12 (2006).

[326] For a more extensive discussion of the clash of doctrines described in this paragraph, see Feldman, *supra* note 13, at 189–208.

[327] *See id.* at 207.

[328] In light of the introduction of more robust forms of post grant review in the 2011 patent reform America Invents Act, a comprehensive approach would also need to consider how those systems interact with Hatch-Waxman and how they could be used for gamesmanship.

From this perspective, the 2009 Biologics Price Competition and Innovation Act ("BPCIA," also commonly known as the "Biologics Act") is not encouraging. The legislation was intended to provide a pathway for swift approval of biosimilars, or what could be called generic biologic drugs, in the same way that Hatch-Waxman provided a speedier pathway for ordinary generic drugs. Biologics are complex cell-derived drugs that include antibodies that fight autoimmune diseases and proteins that boost white blood cell counts during chemotherapy. The Biologics Act, however, is even more complex and convoluted than Hatch-Waxman and seems designed on entirely the wrong template.[329] It took until September 2015—six years after the act's passage—for the first biosimilar to reach the market.[330]

Simplification is not the instinct of lawyers in general nor of patent lawyers in particular. Lawyers are trained to see the nuances in any circumstance and may wish to keep options open for whatever their clients need. Moreover, the patent bar has never been accused of an attraction to exorbitant simplicity. Overcoming these instincts, which are deeply imbedded in the habits of patent stakeholders, will be an essential component of designing a more effective system.

The third step is to let the sun shine in. Both markets and regulators work best when information is fully available—information that invites competition where competition is needed and exposes behavior that regulators can challenge. Moreover, in a world of instant communication, information plays a powerful role in disciplining behavior. Information in pharmaceutical deals and pricing is increasingly segmented, however, and hidden from key players in the industry—whether those players are competitors, regulators, or consumers.

In particular, pharmaceutical pricing is not necessarily drug-specific anymore. Rather, pharmaceutical benefit managers, known as "PBMs," negotiate the prices for the vast majority of commercially insured drug purchases.[331] In other words, PBMs are third-party intermediaries that negotiate drug prices between payers and others. This frequently results in bundled drug pricing, tucked into which may be pricing that reaps supracompetitive rewards or blocks generic competition. For example, a drug company could offer attractive discounts on one drug in exchange for pricing or listing practices that block competition where prices are elevated or competition would be a greater threat.

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[329] *See generally* Jason Kanter & Robin Feldman, *Understanding and Incentivizing Biosimilars*, 64 HASTINGS L.J. 57 (2012) (analyzing and identifying issues with the Biosimilars Act).

[330] *See* Ben Hirschler & Michael Shields, *Novartis Launches First U.S. 'Biosimilar' Drug at 15 Percent Discount*, REUTERS (Sept. 3, 2015, 8:13 AM), http://www.reuters.com/article/us-novartis-drug-idUSKCN0R30C220150903 [https://perma.cc/78K8-GT37] (reporting on the release of a biosimilar version of Amgen's Neupogen).

[331] 149 Cong. Rec. 15,570 (2003).

None of this information is available, either to the market or to regulators. The pharmaceutical ecosystem would benefit tremendously from sunshine rules that require disclosure of PBM pricing deals and rebates. This is not to suggest regulation of pricing, but rather to provide the information that markets and regulators need for efficient functioning.

A fourth step would be to move away from the Supreme Court's rule of reason analysis for pharmaceutical deals that involve generics. Despite the opening that the Supreme Court created in *Actavis*, the lower courts largely have been unable or unwilling to walk through it. The burden remains too great for anyone to bear. Rather, with deals involving generic entry, Congress should place the burden on those making the deals to show that they are proper.[332] The taint of anticompetitive behavior is too strong throughout these arrangements, and the extent to which these deals undermine Hatch-Waxman's intent to introduce generics early and often is too great. One who creates complexity, and the resultant capacity to hide behind that complexity, should have the burden to demonstrate that the effects are justifiable.

The most important step, however, is to make more liberal use of standards-based legal doctrines. The Hatch-Waxman system and its various amendments have tended to focus on precise and particularized legal rules. Brand-name drug companies are forbidden from receiving more than one thirty-month stay; the FDA must take final action on a citizen petition in 150 days.

Some fixes have leaned toward the standards approach. For example, the FDA's ability to deny a citizen petition at any time if it believes a petition was "submitted with the primary purpose of delaying the approval of an application" is an excellent standards-based approach. The amendment granting that power, however, goes on to require that the "petition does not on its face raise valid scientific or regulatory issues,"[333] a provision that moves back toward the realm of rule-based approaches.

A classic standards-based approach can be found in the tax code's step transaction doctrine. The doctrine allows tax authorities to collapse all the steps of a transaction together if the authority deems that they are part of an overall plan by the taxpayer.[334] The doctrine is aimed at ensuring that taxpayers may not avoid legal restrictions by taking individual steps or a circuitous route.[335] A more liberal use of this type of standards-based approach could give courts and regulators the latitude to shut down strategic behavior, as opposed to playing cat and mouse across the regulatory provisions.

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[332] At least two bills have recently been introduced that would begin to shift the burden for some pay-for-delay settlements. *See* Preserve Access to Affordable Generics Act, S. 2019, 114th Cong. (2015); Prescription Drug Affordability Act of 2015, S. 2023, 114th Cong. (2015).

[333] 21 U.S.C. § 355(q)(1)(E) (2012).

[334] *See* Feldman, *Intellectual Property Wrongs*, *supra* note 275, at 310 (describing the value of using this type of doctrine in the patent context).

[335] *Id.*

One should not be overly optimistic. From a political economy perspective, the pressure on members of Congress to avoid an overhaul of the system—let alone a simplified approach that will close off strategic behavior—will be great. When Congress tried to block Hatch-Waxman strategic behaviors in the 2003 amendments to the Act, Congressman Henry Waxman, one of the original authors of the Act, addressed the pharmaceutical industry:

> I call upon the brand-name industry to cease and desist from inventing new games, and that they return to the scientific research that they are good at and that has been their real contribution.[336]

The Congressman's comments appear to have been in vain. Nevertheless, a comprehensive overhaul of Hatch-Waxman, that takes a systems perspective, focuses on simplification, and includes a healthy dose of standards- based authority, could go a long way toward bringing these drug wars under control. After thirty years of experience with Hatch-Waxman, it is time for the next phase.

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[336] FELDMAN, *supra* note 13, at 160 (citing Press Release, Henry A. Waxman, Representative Henry A. Waxman on the Delay of Approval of Generic Drugs (Nov. 20, 2001), http://www.citizen.org/congress/article_redirect.cfm?ID=6496 [https://perma.cc/6VMC-JLQY]).