Empirical Evidence of Drug Pricing Games - A Citizen's Pathway Gone Astray

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For thirty years, the Hatch-Waxman system for expediting approval of generics drugs has brought increased competition to the market and lower drug prices to consumers of all income levels. The generic approval system has enjoyed extraordinary success. Today, more than 80% of prescriptions are filled with generics,⁴ and most generics are eventually priced at a discount that is 80-85% below their brand-name equivalents.⁵ Despite this success, anecdotal evidence has percolated in recent years about new forms of strategic behavior designed to keep drug prices artificially inflated by blocking generic entry.⁶

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⁶ See, e.g., Robin Feldman & Evan Frondorf, Drug Wars: A New Generation of Generic Pharmaceutical Delay, 53 Harv. J. Leg. 499 (2016) (describing what the authors call “generation 3.0” tactics that use administrative processes, regulatory schemes, and drug modification to block or delay generic entry into the market).
In particular, public outcry over the rising price of pharmaceuticals has led to highly publicized congressional hearings, high profile press articles, and outrage from various presidential candidates on the topic. These public forays reveal examples of disturbing behaviors in various corners of the pharmaceutical industry. For example, the nation was riveted when the Turing CEO Martin Shkreli appeared before Congress regarding his company’s elevation of a drug price from $13.50 a tablet to $750 a tablet, a price hike apparently protected by efforts to block out generic competitors. In a similar vein, federal prosecutors are investigating the pharmaceutical company Valeant for tactics related to specialty pharmacies and price increases.

One can understand the motivation behind such behavior. Delaying generic entry for a blockbuster drug—even by a few months—can be worth hundreds of millions of dollars of

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additional revenue. The dollars at stake create a powerful incentive to keep searching for new pathways to delay generic competition. From society’s standpoint, one would prefer that companies search for pathways of treating human disease, rather than pathways of blocking competition. Thus, the process of exposing and shutting down avenues for generic delay is critical for keeping the generic system properly on track.

With the anecdotes described above, as well as recent scholarship, concerns have swirled around the citizen petition process at the Food & Drug Administration (FDA). The FDA’s citizen petition process, and similar programs at other agencies, were created in the 1970s as part of an effort to fashion more participatory regimes, in which ordinary citizens could access the administrative process. The theoretical underpinnings hypothesized that a participatory structure would prevent regulatory agencies from being captured by the very industries they were intended to police. Recent evidence suggests, however, that the FDA’s citizen petition process may have taken a different turn. This study set out to analyze the issue.

From an empirical perspective, we set out to explore whether pharmaceutical companies are systematically using citizen petitions to try to delay the approval of generic competitors. To do this, we looked at the timing of when citizen petitions are filed by competitors during the approval process for generic drugs, as well as trends across time for this type of filing. We were

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9 See Feldman & Frondorf, supra note 6, at 503 and n. 23 (detailing examples).
looking for evidence that such petitions are being used as a last-ditch effort to delay generic entry as long as absolutely possible.

Assembling this information was difficult, to say the least. As with all information about strategic behavior in pharmaceutical pricing, the information must be painstakingly pieced together from scattered and incomplete public records. The article below describes the extensive research undertaken to assemble this picture of a citizen’s pathway being used by drug companies as a delay tactic.

It is a remarkable picture, indeed. Following are the key findings from the study:

- The FDA’s citizen petition pathway is one of the key pathways involved in the modern generation of generic drug delay, playing a role in various game-playing strategies.
- Citizen petitions from competitor companies have essentially doubled since 2003;
- Citizen petitions from competitor companies occupy a striking amount of the process in recent years. Out of all citizen petitions at the FDA (including tobacco, food, dietary supplements, medical devices, etc.) one-in-five is filed by a competitor company asking the FDA not to approve a generic drug.
- Many citizen petitions from competitor companies appear to be a last-ditch effort to hold off generic competition. In fact, the most common grouping of petitions were those filed half-a-year or less before the generic was approved. This is particularly striking given that the overwhelming majority of citizen petitions are denied.\textsuperscript{12} In other words, the results suggest that many competitor petitions are filed late in the process.

\textsuperscript{12} See Carrier & Wander, \textit{supra} note 10, at 249, 274 (finding that the FDA denies 81\% of the citizen petitions related to pharmaceuticals).
game, as a last ditch effort to hold off competition just a little longer, even though they are unlikely to be successful.

- Congressional reforms enacted in 2007 have not stemmed the tide.

The study results provide empirical evidence that the citizen petition process at the FDA has now become a key avenue for strategic behavior by pharmaceutical companies to delay entry of generic competition. Why now? The answer is simple. For decades, pharmaceutical companies had a favored avenue for delaying generic competition. This technique, known as pay-for-delay, is slowly being shut down by the courts in response to cases filed by the Federal Trade Commission and generic companies. With the handwriting on the wall, pharmaceutical companies have looked for other methods of delay. Our results show that the citizen petition process has become a key alternative. It is a far cry from the “participatory citizen” notion that fueled the creation of such avenues at regulatory agencies.

As described above, the delay achieved through a citizen petition, even if the petition is unsuccessful, can be worth hundreds of millions of dollars in revenue for a drug company. The burden of that increased cost ultimately falls on consumers and on the economy.\(^{13}\) Thus, this article provides critical evidence for legislators and regulators in their efforts to ensure adequate competition and appropriate pricing in the health care sector. Finally, following the protocols outlined in the Harvard Journal of Law & Technology Open Letter on Ethical Norms,\(^{14}\) we are making all of our data public for future use by other academics.

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\(^{13}\) See text accompanying notes 15-16, infra.

\(^{14}\) See Robin Feldman, Mark A. Lemley, Jonathan, S. Masur, Arti K. Rai, Open Letter on Ethical Norms in Intellectual Property Scholarship, 29 HARVARD J.L. & TECH. 339 (2016) (signed by dozens of professors). In accordance with the letter, donation information for the University of California Hastings Institute for Innovation Law, where the authors are employed, can be found
Part I of this article briefly describes the process for generic drug entry and details waves of tactics used in the past to block or delay the entry of generic competition. Part II explains the regulatory history of citizen petitions, focusing on changes to the process over time. Citizen petitions have long been a source of consternation for the FDA and other organizations, and a number of modifications have been made in the petitioning process in the hopes of curbing abuse, albeit with mixed success. These changes will factor into our quantitative analysis, as we split our data into periods divided by major changes to the citizen petition regulations.

Part III describes, in detail, the methodology used to obtain and identify all citizen petitions between 2000 and 2012 related to generic drugs as well as every generic drug application approved between 2006 and 2015. These two data sets were then used to “match” citizen petitions with the most relevant generic drug application potentially affected by the petition, setting the stage for a comparison of when citizen petitions are filed relative to the generic drug application filing and approval.

Part IV presents the results of our study, including descriptive statistics about the citizen petitions and generic drug applications we collected. We use dates from citizen petitions and generic drug applications to construct “timing” metrics that show the time that passes between when the generic drug application was filed and when the competitor’s citizen petition was submitted, as well as between when the competitor’s citizen petition was submitted and the generic application was approved, among other calculations.

Part V concludes by examining the nature of the problem and exploring three types of approaches to curb the behavior. These include: 1) a simple prohibition, if one were to conclude that most behavior in the category is likely to be inappropriate; 2) procedural blocks to ensure...
that the behavior cannot create sub-optimal results; or 3) punitive measures as a deterrent. The
section also includes recommendations regarding issues in FDA data collection and
transparency.

I. The Generic Drug Process and Historic Efforts at Delay

A. The Economic Landscape

The advent of generic drugs in the United States has been one of the most significant
sources of cost savings in modern health care. Specifically, the FDA estimates that consumers
saved $217 billion in 2012 through generic competition, and achieved a total of $1.68 trillion of
savings in the decade between 2005 and 2014.\textsuperscript{15} The staggering cost reductions are the result of
both widespread availability of generic drugs and the deep discounts that result in markets with
generic competition. Over 80% of small-molecule drugs have generic equivalents, and more than
80% of all prescriptions are filled using generic medication.\textsuperscript{16} After generic competition begins,
the price of most drugs eventually falls to 80-85% below the original brand-name cost.\textsuperscript{17}

\textsuperscript{15} Generic Pharm. Ass’n, Generic Drug Savings in the U.S. 1 (2013),
supplied by IMS Health); 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.).

\textsuperscript{16} 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
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 51 (Apr.
Entry and Price Competition in Pharmaceuticals in the Quarter Century After the 1984
Brand-name drug companies, who enjoy a monopoly in the market for a drug until generic entry, face a nearly instant plummet in market share and price. Considering that generic entry often coincides with the expiration of a brand-name company’s patents or FDA exclusivities, it is no surprise that looming generic competition is often referred to as the “patent cliff.”18 It is also not surprising that patent holders try to prevent falling into the approaching chasm using any means possible.

Early delay tactics, still in play today, focused on settlements between brand-name companies and potential generic entrants. As described below, the process for generic approval involves a detailed and stylized dance between original drug makers and their would-be competitors, which often results in litigation over the validity of the patent on the original drug or its application to the generic entrant.19 In the course of such litigation, some brand and generic companies have settled their disputes by entering into so-called “pay-for-delay” or “reverse payment” agreements, in which a generic applicant agrees to stay out of the market for a certain period of time in exchange for cash and other considerations. These deals often lead to years of delay and increased revenue valued in the hundreds of millions of dollars.20 From a litigation perspective, these agreements are unusual because they represent a transfer of value from a patent holder to an accused infringer. In contrast, lawsuits generally settle when the accused party agrees to pay an amount.

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18 See, e.g., Carrier & Wander, supra note 10, at 253 (using the term).
19 See text accompanying notes 28-35.
20 For a more detailed explanation and history of delay tactics, see Robin Feldman & Evan Frondorf, Drug Wars: A New Generation Of Generic Pharmaceutical Delay, 53 HARV. J. ON LEGIS. __ (2016).
The companies have argued that such settlements represent a reasonable assessment of the cost of continuing litigation and risks of losing a case, no matter how strong one’s position may be. Antitrust scholars and competition authorities have raised concerns, however, that such agreements allow the parties to keep prices artificially high and then share the resulting monopoly rents.\(^{21}\) Brand name companies are able to preserve years of monopoly sales, and generics receive a share of those profits from the settlement payment, generally worth more than what they might make in a duopoly or in a competitive market.

Most important, with benefits provided under Hatch-Waxman to the first generic filer, a pay-for-delay agreement frequently serves as a roadblock to any other competitors, preserving the monopoly-rent environment. In light of these effects, the FTC has estimated that reverse payment settlements cost consumers upwards of $3.5 billion each year.\(^{22}\)

After years of debate and scrutiny of reverse payment settlements, the Supreme Court entered the conversation in *FTC v. Actavis.*\(^{23}\) While declining to find pay-for-delay agreements presumptively illegal, the Court allowed an FTC case challenging a reverse payment to go forward and outlined a number of reasons why reverse payment settlements should be open to


antitrust scrutiny. In the antitrust world where the law moves at a glacial pace, the Supreme Court’s pronouncement was the equivalent of a minor temblor. The shock waves have filtered slowly through the lower courts, as they have shaped the contours of antitrust analysis and ruled on what kinds of agreements should be subject to scrutiny. In particular, pharmaceutical companies have developed agreements far more complex than what the Supreme Court ruled on in Actavis, including ones that eliminate pure cash payments and provide consideration such as promotional deals, licensing agreements, research and development deals, and the settlement of multiple cases at once.

Although the topic continues to percolate through the courts, pay-for-delay agreements appear to be on the decline. In the first full year after the Actavis decision, the FTC labeled 21 settlements as potential pay-for-delay deals in fiscal year 2014, down from 29 in fiscal year 2013 and the record high of 40 in fiscal year 2012.

With settlements between brand-name companies and prospective generics coming under this substantial scrutiny in recent years, pharmaceutical companies have turned to new tactics to delay generic entry. These strategies make use of public FDA petition processes, inconsequential labeling changes, slight tweaks to existing drugs and formulations, and disingenuous safety concerns, among others, to block generic competition and obtain additional months of monopoly power. The move has been from collaboration with generic drug-makers to obstruction of generics. Even if these tactics are likely to fail in constructing a permanent generic blockade,

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25 See Robin Feldman, Ending Patent Exceptionalism and Structuring the Rule of Reason: The Supreme Court Opens the Door for Both, 1 Minn. J.L. Sci. & Tech. 61 (2014); see also Michael A. Carrier, Payment After Actavis, 100 Iowa L. Rev. 7 (2014); Aaron Edlin et al., Activating Actavis, 28 ANTITRUST 16 (2013).
they are relatively costless and easy to attempt; and even if they only secure a few months of last-ditch delay, those precious few weeks could still be worth hundreds of millions of dollars, given that top-selling drugs may exceed $1 billion in U.S. sales annually. The strategy is similar to futile measures to slow a sinking ship by tossing everything overboard; the outcome is essentially inevitable, but the timing is malleable. In this case, however, slowing submersion, even marginally, can be extremely valuable.

B. The Generic Approval Process:

Understanding pharmaceutical game-playing techniques requires at least a basic understanding of the process for approval of generic drugs. The passage of the Hatch-Waxman Act in 1984 ushered in the modern era of generic medication through a number of regulations designed to ease the path of generics to the market. The Act introduced the concept of the Abbreviated New Drug Application, commonly referred to as an “ANDA,” which allows prospective generics to use existing clinical trial data to obtain approval of a drug bioequivalent to an existing drug. The development process can be completed without the threat of a patent infringement suit from the drug company already on the market.

Although the term “ANDA” is familiar to those in the life science industry, we use the term “generic drug application,” to avoid the confusion of a paper littered with insider acronyms.


As one of the authors has noted in the past, writing in clear, simple language presses legal actors to be faithful to supportable logic, rather than subject to the whims of prejudice masked in obscurity.\(^{29}\)

In addition to an expedited approval process, Hatch-Waxman offers incentives for generics to challenge weak or invalid patents protecting drugs already on the market. The process begins with what is known as the “Orange Book.” When an original drug-maker applies to the FDA for approval, the company is required to identify all patents protecting the drug. That list is publicized in an FDA document commonly known as the “Orange Book,” in reference to the orange cover on each volume.\(^{30}\)

When a generic company applies for permission to make a generic version of the drug down the road, the generic applicant must make a certification in relation to each of the patents listed in the Orange Book, declaring, among other options, that the patent is expired, irrelevant, or that the applicant will not enter the market until the expiration of the patent.\(^{31}\) One category of certifications, however, holds most of the action. So-called “Paragraph IV” certifications declare that one of the patents listed in the Orange Book is either invalid or will not be infringed by the

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\(^{29}\) See Robin Feldman, *The Role of Science in Law*, 180 174-195 (Oxford 2009) (excerpted in Plain Language Patents, 17 Texas I.P.L.J. 289 (2009) and discussing the dangers that arise when legal actors cloak themselves in scientific jargon); see also id. at 5-7, 174-195 (exploring the issue further).


generic drug application. A Paragraph IV certification initiates a stylized dance between the parties that generally results in litigation.

The process contains an incentive to encourage generic applicants to file Paragraph IV certifications declaring that one of the original drug-maker’s patents is invalid or invalidly applied. The first generic company to submit such a certification is, with some stipulations, entitled to six months of marketing exclusivity for the generic drug, as long as the generic does not lose its patent infringement case. Thus, the first generic that meets this criteria will be the only competitor to the brand name drug for its first 6 months on the market, a period that can be worth hundreds of millions of dollars in exclusive sales. No other generic will be approved during this valuable exclusivity period, and the benefit can be worth hundreds of millions of dollars in exclusive sales. The benefit reflects concern over the presence of invalid patents.

33 See generally sources cited at n. 27, supra.
34 21 U.S.C. § 355(j)(5)(B)(iv). After 2003 amendments to Hatch-Waxman, it is possible to forfeit the 180-day exclusivity period without losing a patent infringement case when certain criteria are met, such as a failure to market the generic within a certain period of time. 21 U.S.C. § 355(j)(5)(D). 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.
35 In fact, sales during this period can represent the majority of profits that can be potentially gained from generic entry. Matthew Avery, Continuing Abuse of Hatch-Waxman Act by Pharmaceutical Patent Holders and the Failure of the 2003 Amendments, 60 Hastings L.J. 171, 178 & 178 n. 55 & 56 (2008). As the number of competitors in a market increases, the price drops to the point where it approaches the marginal cost of producing the drug, thus nearing perfect competition and minimizing the amount of profit that any one seller can obtain. During the 180-day period, the FDA is not permitted to approve any other generic applications that have a Paragraph IV certification. 21 U.S.C § 355(J)(5)(B)( iv)(I)-(II). However, this does not entirely prevent the presence of other competition. Brand-name companies have developed a technique in which they 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.” See Feldman & Frondorf, supra note 6, at 522-524 (describing authorized generics in detail); FED. TRADE. COMM’N, Authorized Generic Drugs: Short-Term Effects and Long-Term Impact (2011), available at http://www.ftc.gov/os/2011/08/2011genericdrugreport.pdf.
within the system and is intended to give generic companies an incentive to do battle with pharmaceutical companies whose patents are weak or applied to the wrong product.\textsuperscript{36}

Data on the results of Paragraph IV court cases confirm the presence of weak patents within the life science arena and the importance of the Paragraph IV process. For example, a Federal Trade Commission study of all such cases resolved on the merits between 1992 and 2000 found that the generic company prevailed 73\% of the time.\textsuperscript{37} Cases resolved on the merits represent only a portion of the Paragraph IV certifications.\textsuperscript{38} Nevertheless, the FTC study offers striking evidence that, like high tech, life sciences also must worry about weak patents.\textsuperscript{39}

Hatch-Waxman led to the rapid proliferation of generics. The complexity of the system also created an environment ripe for abuse. From the pay-for-delay deals described above to other manipulations, courts, legislators, and regulators have engaged in an endless game of cat-and-mouse to close off avenues for manipulation as they are uncovered.\textsuperscript{40} The road now leads to the lowly citizen petition.

In \textit{Drug Wars: A New Generation of Generic Pharmaceutical Delay}, authors Feldman and Frondorf refer to the idea of “Generation 3.0” — this most recent collection of generic delay strategies, connected by their efforts at obstruction of generics rather than collaboration between pharmaceutical companies. Our survey of all citizen petitions filed between 2000 and 2012 makes it clear that citizen petitions do not represent just one of these strategies; rather, petitions

\begin{itemize}
\item \textsuperscript{36}See Feldman, \textit{supra} note 21, at 161.
\item \textsuperscript{38}Cf. Robin Feldman, Tom Ewing, \& Sara Jeruss, \textit{The AIA 500 Expanded: The Effects of Patent Monetization Entities}, 18 UCLA J.L. \& TECH. 1, 59-60 (2013) (empirical study of roughly 13,000 patent lawsuits across 4 years showing, among other findings, that most patent lawsuits settle prior to a decision on the merits).
\item \textsuperscript{39}See also Feldman, \textit{supra} note 21 (discussing evergreening patents).
\item \textsuperscript{40}See generally, Feldman \& Frondorf, \textit{supra} note 6.
\end{itemize}
are the gateway to many identified forms of delay. Labeling changes that create more work for
generics, requests to institute a safety-related “REMS” program of restricted distribution for a
drug — many of these tactics are initiated through citizen petitions. Thus, short, cheap filings
with the FDA — citizen petitions — are perhaps the most prominent way that small-scale,
obstructionist delay is effectuated today.

II. Citizen Petitions

The citizen petition process was mandated by Congress’ passage of the Administrative
Procedure Act, which requires federal agencies to create a formal route for the public to petition
the agency to change, amend, or repeal an agency rule. As described above, the FDA’s citizen
petition process can be traced back to the 1970s, a period in which courts and policy-makers
encouraged the creation of pathways so that ordinary citizens could engage in the administrative
process taking place at regulatory agencies. The FDA’s process allows petitioners to “request
the Commissioner of Food and Drugs to (issue, amend, or revoke a regulation or order or take or
refrain from any other form of administrative action).” Petitions must state all factual and legal

42 See sources cited supra note 11.
on the standard citizen petition also exists, known as a “petition for stay of agency action.” These
petitions request that the FDA delay enforcement or the effective date of an administrative
action. 21 CFR §10.35, https://www.law.cornell.edu/cfr/text/21/10.35. They function and are
governed similarly to citizen petitions, so we have grouped them together for the purposes of this
paper, a categorization that the FDA has used as well. FDA 2009 Report of 505(q) p.8. (“Both
citizen petitions and petitions for stay of agency action will be collectively referred to as
‘petitions’ throughout this report.”)
grounds for the petition, provide all relevant information (including that which may be unfavorable), and add an environmental or economic impact section if necessary. The agency must make a final grant or denial of the petition.

On its face, the citizen petition process should be a useful method for ensuring that the public can communicate concerns to a key regulatory agency. A mechanism designed for concerned citizens and scientists to raise questions about drugs, food, and FDA regulations, however, has seemingly turned into a playground for pharmaceutical companies to challenge drug applications, especially those related to pending generic applications. In many cases, the “concerned citizen” behind a petition is actually a large pharmaceutical company, seeking to stop or delay approval of a generic drug through a variety of different arguments. These include direct attacks against the generic’s application and its bioequivalence or clinical data; appeals to safety; calls to preserve or add new exclusivities for the brand-name drug; and more. Some petitions raise important or necessary issues; many others, however, seem frivolous or questionable in their aims.

A. Troubling Behavior in the Citizen Petition Process

As an example of a troubling citizen petition, consider the petition we uncovered that was filed in 2007 by Mutual Pharmaceuticals, a company the FDA had already approved for selling a

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45 Id. at E. (e)(1)
generic version of the blood pressure medicine, felodipine.\(^{46}\) The petition sought to delay other generic companies from gaining approval. Specifically, the petition requested that the FDA not approve any new generic applications while it decided whether warnings should be added to the current drug labels regarding whether products containing certain forms of orange juice might affect absorption of the drug.\(^{47}\) Among other requests, the petition also suggested that all new generic drug approvals should be delayed while the FDA asked the original drug maker to specify which form of orange juice was used in its studies.\(^{48}\) Of course, as a currently approved seller of generic felodipine, the company writing the citizen petition would be free to continue selling with the existing labels and based on the existing study information.

Mutual Pharmaceuticals explained that its citizen petition was motivated by a study showing different effects of Seville orange juice versus “regular” orange juice on metabolism. The FDA, however, was unimpressed.\(^{49}\) In its response to the petition, the Agency stated, “we do not believe that the results of the Malhotra study present a serious safety concern.”\(^{50}\) In fact, the FDA seems to have a clear disdain for the claims made in the petition:

[Y]ou hypothesize that there may be clinical consequences associated with the coadministration of felodipine and components of Seville orange juice consumed in this form. You have offered no data to support this hypothesis. In fact, we searched the Adverse Event Reporting System (AERS) database and found no reported interactions between Seville or bitter orange products and any drug product.\(^{51}\)

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\(^{46}\) See [https://www.regulations.gov/#!documentDetail;D=FDA-2007-P-0123-0009](https://www.regulations.gov/#!documentDetail;D=FDA-2007-P-0123-0009). Felodipine is also branded as Plendil.


\(^{48}\) See id.

\(^{49}\) [https://www.regulations.gov/#!documentDetail;D=FDA-2007-P-0123-0002](https://www.regulations.gov/#!documentDetail;D=FDA-2007-P-0123-0002), p.2

\(^{50}\) [https://www.regulations.gov/#!documentDetail;D=FDA-2007-P-0123-0009](https://www.regulations.gov/#!documentDetail;D=FDA-2007-P-0123-0009), p.4. The FDA did grant Mutual’s request that a portion of the brand-name Plendil labeling stating that “[o]range juice does not appear to modify the kinetics of Plendil” be qualified to not imply that orange juice has no effects on the kinetics of Plendil, even if the minimal effect does not appear to effect the safety or efficacy of the drug. p.4

\(^{51}\) p. 4 of denial
In a footnote, the FDA hints at skepticism over Mutual’s motives for filing the petition, questioning the truthfulness of Mutual’s affirmations: “You have certified that you first became aware of the information upon which you have based Petition 1 (e.g., Malhotra study) on November 5, 2007. We note, however, the Malhotra study was published in 2001 and predates approval of Mutual’s [generic application].”

Unsurprisingly, Mutual was the first company to receive approval to sell generic felodipine, receiving approval from the FDA in 2004. The next generic application was filed by Mylan in the first quarter of 2007, just months before Mutual felt moved to file its citizen petition. The FDA denied the citizen petition the following year, on April 17, 2008 — the same day that Mylan’s generic application was approved. The timing indicates that Mutual’s “orange juice petition” was one of the last barriers to final approval. Thus, a last-minute baseless petition about types of orange juice cost consumers untold millions in the delay it posed to the approval of a second generic for felodipine.

The example we uncovered with felodipine fits the rumors swirling about the current modus operandi for citizen petitions — pharmaceutical companies make a facially interesting, scientific-sounding claim (Seville orange juice does increase absorption and peak drug concentration, after all) timed to the months right before ANDA approval, and the claims are

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52 p. 3 footnote 3 of denial
53 Cite to our database, ANDA No. 78855
54 p. 1 of FDA denial, Drugs@FDA approval info for ANDA No. 78855.
55 For example, sales of Plendil were $251 in 2007, even with a generic already on the market. See Mylan Corp Press Releases, available at http://newsroom.mylan.com/press-releases?item=122579
eventually denied by the FDA. Despite the eventual denials, the delays cost consumers untold sums and waste governmental resources.\textsuperscript{56}

**B. Changes to the FDA Citizen Petition Process:**

After years of hearings and debate on numerous FDA regulatory issues, Congress passed the Food and Drug Administration Amendments Act (FDAAA) in 2007. The Act included the largest reform of the citizen petition process in the program’s 30-year history.\textsuperscript{57} These changes came in response to a variety of concerns with citizen petitioning at the FDA, ranging from increasing petition backlogs to signs that the process was being used inappropriately to delay entry of generic drugs. The amendment was aimed at curbing attempts to derail the generic drug approval process and delay the entry of generics.\textsuperscript{58}

Specifically, the 2007 Amendments added subsection “(q)” to section 355 of U.S. Code Title 21, where most of the legislation relating to generic applications already resided. This new provision generally is called “505(q)” in academic and regulatory discussions, and the petitions that fall under it are called “505(q) petitions.”

\textsuperscript{56} See, e.g., Carrier & Wander, supra note 10, at 252, 283-285 (detailing the saga of a citizen petition that delayed generic entry of the depression drug Wellbutrin XL for 133 days, costing consumers $600 million).


\textsuperscript{58} See Carrier & Wander, supra note 10, at 263 (discussing testimony of Senator Edward Kennedy that, “[t]he citizen petition provision is designed to address attempts to derail generic drug approvals. Those attempts, when successful, hurt consumers and the public health” 153 Cong. Rec. 25,047 (2007)).
Section 505(q) applies a new set of regulations to all citizen petitions that ask the FDA to take action related to a pending generic application. Most notably, the section requires that the FDA respond to all such petitions within 180 days. In 2012, this deadline was shortened further to 150 days through amendment in the Food and Drug Administration Safety Act (FDASIA). Approval of a generic application cannot be delayed because of a citizen petition beyond the 150- or 180-day review period, unless it is determined that a delay is necessary for public health reasons.

Most important, Section 505(q) contains provisions intended to deter those who would file citizen petitions in an effort to delay generic competition. Thus, if the citizen petition falls under 505(q) as relating to a generic application, the person filing the citizen petition must certify that the petition is not frivolous, all information favorable and unfavorable has been provided, and the petition was not intentionally delayed. The citizen petition also must provide the date when the filer first became aware of the concern and the names of those who are funding the petition.

Finally, 505(q) gives the FDA the power to summarily deny any petition it believes was filed with the “primary purpose” of delaying generic approval if the petition also does not “on its

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59 505(q) covers citizen petitions related to two categories of FDA approval applications. These are abbreviated new drug applications (ANDAs) and other forms of applications that rely on investigations not performed by or for the applicant. The latter form is referred to as 505(B)(2) applications. See http://www.fda.gov/downloads/Drugs/.../Guidances/ucm079345.pdf
60 21 U.S.C. §355(q)(1)(F)
61 Food and Drug Administration Safety and Innovation Act, Pub. L. 112-144, 126 Stat. 993 (2012). The FDASIA also extended the stipulations of section 505(q) to biosimilar applications, which are beyond the scope of this paper.
Together, the provisions of section 505(q) were meant to put an end to the abuse of citizen petitions by pharmaceutical companies.

The major changes to the citizen petition process beginning in 2007 serve as a natural break point in our data, allowing us to observe any effects of the legislation along with trends across time. In addition, some of the data reports mandated by the 2007 Amendments provide interesting information for our exploration.

III. Methodology

A. Overview

As described above, anecdotes have swirled for a number of years that drug companies are abusing the citizen petition process as a delay tactic to keep generics off the market. We set out to take a quantitative look. Specifically, our goal was to explore empirically whether pharmaceutical companies are systematically using the citizen petition process to delay entry of generic drugs.

To approach the question, we sought to analyze the timing of when citizen petitions are filed during the generic drug approval process and the frequency with which petitions that have the potential to delay are filed. We hypothesized that such petitions would be filed towards the

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65 See, e.g., Feldman & Frondorf, supra note 6; Ameet Sarpatwari, Jerry Avorn, & Aaron Kesselheim, Using a Drug-Safety Tool to Prevent Competition, 370(16) NEW ENGLAND J. OF MED. 1476, 1477 (April 17, 2014) (discussing Citizen Petition from Celgene Coporation to the FDA 17-18 (September 20, 2007), available at https://www.regulations.gov/document?D=FDA-2007-P-0113-0002). Most important, Carrier & Wander, who documented a rise in citizen petitions in general, suggested that the rise might be a sign of delay behavior. See Carrier & Wander, supra note 10 (documenting empirically a rise in citizen petitions and detailing two anecdotal examples of petitions that resulted in delay, one related to the depression drug Wellbutrin and one related to the insomnia drug Ambien).
end of the approval process to put up one more roadblock on the way to a successful approval of a generic drug.

Assembling information such as this from the files made public by the FDA is tremendously difficult. Although the FDA publishes a large amount of information on its public website, and more in hard copy through its Orange Books, much important information is missing. Such information must be pieced together, estimated, or in some cases, simply cannot be located. As will be described in more detail below, for example, the FDA does not publicly reveal the dates when generic applications are filed. We were able to track down many of those dates, however, by reading PDFs of various letters in the files of applications that had been approved. Most important, we developed a method of identifying the likely quarter in which an application was filed by working from the FDA’s file numbering systems.

The FDA citizen petition files also do not link to or indicate which generic application the petition relates to, information that is important for tracking the timing of citizen petitions in relation to the application process for a particular generic drug. Moreover, prior to 2007, the FDA citizen petition files do not indicate at all whether the petitions are related to a generic application. We wanted to assemble a data set of citizen petitions that have the potential to delay generic applications with links to the relevant generic application and timing data. All of this information also had to be assembled by hand, piecing together information in the citizen petition letters and the various generic application files.

Through this process, we were able to assemble relevant data sets including 1) generic applications filed between the beginning of 2000 and the end of 2012 for which the generic company has now received approval to market, along with the quarter in which they were first

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66 See text accompanying notes 29-30 (explaining “Orange Books”).
filed and the date upon which they were approved and 2) citizen petitions that appear related to those generic applications, along with the dates on which the citizen petition was filed and the date of the FDA’s response. These sets of data allowed us to analyze the timing of when citizen petitions are filed during the generic drug approval process and the frequency with which petitions that have the potential to delay are filed. In simplified form, the process can be summarized as the following:

- 1) We compiled all citizen petitions and related documents from 2000 to 2012.
- 2) We identified citizen petitions related to pharmaceuticals, with a particular focus on generic drugs.
- 3) We read each remaining citizen petition and classified which petitions were related to generic drugs or had the power to delay generic approval, regardless of the merits or circumstances of the petition.
- 4) We constructed a data set of all generic applications approved during the relevant period, pulling approval dates and filing dates when available from PDFs of letters within the files. For generic applications without filing dates, we were able to estimate a filing date down to the quarter-year for most drugs.
- 5) We matched each citizen petition with the generic application most relevant to the requests made in the petition.
- 6) Using these citizen petition-generic application pairs, we constructed metrics with the goal of isolating the timing of petitions during the generic drug approval process.

The subsections below describe the process in detail. As will be evident from the description, collecting and assembling the data required extensive effort. The amount of effort
required to extract the information from public sources, along with our commitment to open and ethical academic data, prompted us to make the data sets fully available to the public. We hope other academics will be able to use the data for future research.

B. **Methodology Details:**

Section III.A above described the methodology in overview. The following subsections describe the process in detail.

1. **Compiling All Citizen Petitions Since 2000**

To begin our analysis, we compiled all documents related to citizen petitions that were filed with the FDA between the beginning of 2000 and the end of 2012. We limited our search to citizen petitions filed prior to 2013 because test analyses indicated that citizen petitions filed between 2013 and 2016 frequently relate to drugs that have not yet been approved. Without final approval files, one cannot find much of the information necessary for the analysis, nor would one be able to reach timing conclusions when the generic application is still in progress.

The citizen petition documents were obtained using two sources. The first is an application program interface made available by Regulations.gov, a website provided by the federal government to serve as a searchable repository for regulatory documents. The interface allows data to be queried and stored in formats easily accessible to data analysis languages. For the years 2000-2012, we obtained 19,520 documents. Multiple documents, however, can correspond to one citizen petition docket number. For example, supplemental data, support letters, and the FDA’s actual response are different types of documents that could be listed

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separately but correspond to a single citizen petition. The 19,520 documents were linked to approximately 1,790 citizen petition citizen petitions filed between 2000 and 2012 and archived online.

One should note, however, that the FDA’s database on Regulations.gov may be incomplete. In addition, if the FDA’s database has inconsistent labeling, the search may not have picked up every document. We are aware of at least a few citizen petitions that do not appear from our search of Regulations.gov because the FDA did not digitally categorize them as citizen petitions, which we added into our data set.68

The second source is the FDA Law Blog’s citizen petition tracker, which keeps a record of citizen petitions that are related to generic drug applications.69 FDA Law Blog is a privately assembled data set this is available to the public. This data set, however, only reaches back to partway through 2008. When using data from FDA Law Blog, we hand-checked each of the blog’s inclusions and sampled the blog’s exclusions each year, testing them against our own sorting of the information available on line from the regulatory agency itself. We found no errors in the FDA Law Blog’s data, and we believe it identifies a small number of citizen petitions that the government site, Regulations.gov, fails to label online as citizen petitions.

2. Identifying Citizen Petitions that Could Delay Generic Competition

With the full data set of citizen petitions, we turned to identifying citizen petitions that had the power to delay pending or forthcoming generic applications. This process involved two steps for removing non-relevant petitions: 1) removing petitions whose titles or categories

68 See text accompanying notes 69-70, infra (describing accessing and cross-checking through the FDA Law Blog).
69 http://www.fdalawblog.net. Once again, a similar method was used for verification by Carrier and Wander in their empirical look at citizen petitions.
indicated on their face that they were unrelated to delay of generic competition; and 2) removing petitions through viewing the docket in full.

a. Removing Citizen Petitions Unrelated on Their Face:

As a first step in eliminating citizen petitions unrelated to our inquiry into delaying generic drug entry, we removed petitions regarding other areas of FDA oversight. These included citizen petitions related to food (e.g. “Revise The Labeling Requirements for Eggs Sold In the United States”), medical devices (e.g. “Reclassification for Mobile Bearing Knees from Class III and Class II”), tobacco (e.g. “Reclassify Nicotine Vaporizers (E-cigarettes) from ‘Drug-Device Combination’ to ‘Tobacco Product’”), and dietary supplements (e.g. “Treat Weight Loss Claims for Dietary Supplements as Disease Claims”). After filtering all of the above categories of petitions, the 1,790 petitions from 2000-2012 were narrowed to 1,158. Thus, 65% of all citizen petitions filed at the FDA during the relevant 13 years were in some way related to pharmaceuticals.

The next step involved removing drug-related petitions whose docket titles revealed that they most likely were unrelated to the possible obstruction of Hatch-Waxman generic drug competition under consideration in our study. Thus, petitions related to biologic drugs were excluded. Biologic drugs are complex medications—such as antibodies, hormones, and proteins—that are derived from cells. Unlike the small-molecule drugs with which most patients are widely familiar—such as aspirin—biologics and their generic “biosimilars” undergo a separate approval process governed by a regulatory structure other than Hatch-Waxman.\(^7^0\) The biosimilar process differs substantially from Hatch-Waxman and is in its infancy. In fact, the

\(^7^0\) See 42 U.S.C. 262 (codifying the Biologics Price Competition and Innovation Act, signed into law in 2010).
FDA approved the first biosimilar, in March of 2015, well beyond the 2000-2012 period of our study. Thus, analyses of potential delay tactics in the biosimilars regulatory pipeline are better suited for a different paper.

Petitions related to the approval of new animal drugs or generic animal drugs also were removed, given that they exist in a different class than standard small-molecule medications. We also chose to eliminate citizen petitions filed by third-party advocacy groups, rather than competitors, because we were looking for efforts by competitors to derail competition. An example is a petition titled “Add a Black Box Warning About the Increased Risks of Heart Attacks and Other Cardiovascular Dangers to the Product Labels of all Testosterone-Containing Drugs Presently on the Market in the U.S.,” filed by “Public Citizen,” an advocacy group and think tank.

One cannot eliminate the possibility that third-party groups such as these might collude with a pharmaceutical company or be unwittingly roped into behavior that has the happy coincidence of benefitting an anticompetitive goal. Elements of the pharmaceutical industry have, indeed, taken heat in recent years for efforts to influence and for financing of academics and third-party groups. Given the source of these petitions, however, and the fact that this set of petitions rarely singled out specific generics, we chose not to include safety-related petitions filed by third-parties in our analysis of timing relationships.

We also removed two defined categories of drug petitions that are most often filed by prospective generics seeking a route to the market — moves that promote competition rather

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72 https://www.regulations.gov/#!docketBrowser;rpp=25;po=0;D=FDA-2014-P-0258
73 See Feldman, et. al., supra note 14, at 341-343 (describing conflict of interest examples in life science research).
than seeking to restrict it. The first of these are “ANDA suitability” petitions. A suitability petition is a request from a potential generic manufacturer to file an approval application for a drug that differs slightly from the original reference drug in characteristics such as route of administration, dosage form, and strength.\textsuperscript{74}

The second is a “discontinuation petition,” which could also be described as a “withdrawal determination petition.” When a drug is discontinued or removed from the market, the FDA must ascertain whether the drug was removed for reasons of safety or effectiveness before allowing it to be referenced in a generic application. Generic hopefuls can file a discontinuation petition asking the FDA to make this determination so a generic application can be filed.\textsuperscript{75} Given that both suitability and withdrawal petitions by definition are designed to allow additional generic entry, rather than to block or restrict entry, they were removed from our final database.

\textbf{b. Removing Citizen Petitions Unrelated from Their Content}

As a second step in eliminating citizen petitions unrelated to our inquiry, we viewed each remaining petition docket in full. The number of documents available in each docket varies considerably, and we used all available materials to make a determination, including the petitions, interim FDA correspondence, and the FDA’s response as available. As described above, our goal was to look at timing, not to make our own judgment of the legitimacy of any particular issue raised.

\textsuperscript{74} \url{http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ManualofPoliciesProcedures/UCM365676.pdf}
\textsuperscript{75} 21 CFR 314.161 (a)-(e).
Once again, we looked to eliminate citizen petitions that had little or no relation to pending or approaching generic drug applications or were unrelated to the possibility of delay. Thus, we eliminated citizen petitions that would meet criteria used in the previous section for deletion but were not immediately apparent from the docket title, such as “ANDA suitability,” withdrawal, and third-party safety petitions.

In addition, citizen petitions related to new drug applications (NDAs) were taken out of the final database, given that they are generally unrelated to generic drug competition. One important exception is a specific category of new drug applications classified as “505(b)(2)s.” Section 505(b)(2) applications fall somewhere between a pure applications for a new drug and applications for a generic drug. They are similar to filing an “ANDA suitability” petition in that both rely on existing data from existing drugs but involve drugs that differ from the existing ones in some aspect, such as formulation, dosage, treatment indication, and over-the-counter status, among others.76

As described above, we chose to eliminate ANDA suitability petitions from our data set on the theory that these represent an attempt by a generic company to broaden competition by seeking entry. In contrast, the 505(b)(2) citizen petitions that we kept within the data set here represent attempts by other companies to block the entry of drugs—ones that are closely related

76  See text accompanying note 74, supra (describing ANDA suitability petitions); http://www.fda.gov/downloads/Drugs/.../Guidances/ucm079345.pdf. New drug applications (NDAs) fall under section 505(b)(1) and generic drug applications (ANDAs) generally fall under section 505(j). In fact, suitability petitions and 505(b)(2)s are quite similar in the types of drugs that are eligible, but the differing processes (petition vs. application) appeal differently to generic companies depending on individual circumstances. Furthermore, the proposed differences in a drug implicated in a suitability petition cannot require new evidence that the new drug is safe and effective. An example of change that might not raise safety or effectiveness questions is when a generic proposes to sell an intermediate dosage of an approved drug — say, a 300mg tablet when 200mg and 400mg tablets are already approved for the brand-name version of the drug. http://blog.camargopharma.com/index.php/2009/06/12/anda-suitability-petition-vs-505b2/.
to already-marketed pharmaceuticals and go through an approval process similar to approval for generic drugs. Thus, we choose to keep those citizen petitions in the data set.\textsuperscript{77}

Similarly eliminated were those that refer to drugs already on the market, often requesting to declare a drug “misbranded” or require labeling charges. Since these petitions refer to generic applications that have already been approved, they generally do not have the potential to \textit{delay} generic approval, although they could potentially cause removal of the drug from the market.\textsuperscript{78}

Finally, when the relation to generics was tenuous or unclear, we chose not to include the petition in our data set. For example, a number of petitions referred to a generic company’s request to allow a drug to certify to multiple branded drugs, requests to list or delist patents from the Orange Book, and so on. Similarly eliminated were those that refer to drugs already on the market, often requesting to declare a drug “misbranded” or require labeling charges. Since these petitions refer to generic applications that have already been approved, they generally do not have the potential to \textit{delay} generic approval, although they could potentially cause removal of the drug from the market.\textsuperscript{79} While it is possible that some of these petitions we considered to

\textsuperscript{77} Notably, the Section 505(q) requirements added in the 2007 Amendments apply to citizen petitions related to both ANDAs and 505(b)(2) applications. See FDA 2009 Report on 505(q) p. 8-9. See also text accompanying notes 57-Error! Bookmark not defined., supra (describing the 2007 Amendments and Section 505(q)).

\textsuperscript{78} This criterion is generally in line with current law and the guidance the FDA released interpreting the provisions of section 505(q) of the 2007 amendments. First, 505(q)(1)(A) specifically refers to pending applications, and the FDA has interpreted the amendments to say that section 505(q) applies “only to petitions for which, at the time the petition is submitted, at least one ANDA, 505(b)(2) application, or biosimilar application related to the subject matter is pending.” See FDA 505(q) guidance 2014 p.6

\textsuperscript{79} This criterion is generally in line with current law and the guidance the FDA released interpreting the provisions of section 505(q) of the 2007 amendments. First, 505(q)(1)(A) specifically refers to pending applications, and the FDA has interpreted the amendments to say that section 505(q) applies “only to petitions for which, at the time the petition is submitted, at
have a tenuous connection may have been part of a generic delay scheme, our goal was to be as careful and conservative as possible, and to err on the side of understating any results we might find.

c. The Final Citizen Petition Pool

After removing the citizen petition categories described above, the pool that remained include those petitions that have the potential to delay a pending or forthcoming generic competitor. The decision to include a citizen petition in the data set was based solely on the topic of the petition, and no attempt was made to judge the merit of the issues raised in gathering the group. The final group is composed of the following:

Many of the citizen petitions in the final pool specifically ask the FDA to stay or delay approval of a generic application. These citizen petitions frequently raise concerns about safety or incomplete bioequivalence or clinical testing, with bioequivalence testing as a particular prevalent topic. Many of these petitions ask the FDA to stay approval of a generic drug until the applicant demonstrates something that the Agency already requires for approval of a generic drug. This type of petition essentially forces the FDA to make a redundant ruling that a certain type of testing is required, when in fact, that testing is already required.

These redundant testing petitions lead to a number of FDA rulings actually granting a petition while not actually imposing any new requirements on the generic applicant. The result

least one ANDA, 505(b)(2) application, or biosimilar application related to the subject matter is pending.” See FDA 505(q) guidance 2014 p.6
may be a petition that is granted in part and denied in part, with the granted portion no more than a formality that lacks practical significance.\(^80\)

Consider the FDA’s response to a citizen petition that requested a stay of generic versions of Argatroban, a drug to prevent blood clotting. In its response, the FDA acknowledges that the actions granted in the petition are merely those already required under FDA policy, stating that “[t]o the extent it is consistent with our current policies, we grant your request.”\(^81\)

Other citizen petitions remaining in the pool ask that the FDA direct a generic applicant to re-file its application in a different form, changing it from an ANDA (the category that for applications that reference an existing drug) to a 505(b)(2) (the category for applications that reference an existing drug but differ slightly in formulation, dosage, treatment indication, etc.) or demand that a generic applicant revise its application to make Paragraph III or IV certifications to additional patents. All of the requests would add additional burdens on a generic applicant to comply. Thus, they are best classified as petitions with the potential to delay generics.

For example, one petition uses a bioequivalence issue to suggest that “the Agency require the applicant(s) to withdraw the ANDA(s) and resubmit it as an application(s) under section 505(b)(2) of the FD&C Act unless the ANDA applicant product is formulated with rsCT and is bio-identical in terms of biological impurities and an in vivo bioequivalency study has been completed and has met all bioequivalency criteria.”\(^82\) Such a request could represent a legitimate concern, or it could be a redundancy request, that is, asking the FDA to require that the generic

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\(^80\) See Carrier/Wander p. 266 (PDF p. 18); see also id. at 261 (noting that the FDA’s Director of the Office of Generic Drugs has made a similar observation, saying, “when petitions are granted, in whole or in part, it is often because the FDA already has the proposed scientific or legal standard in place or is already planning to take the action that the petition requests”).


\(^82\) See, e.g., petition FDA-2008-P-0616https://www.regulations.gov/#!documentDetail;D=FDA-2008-P-0616-0001(among other demands in the petition).
applicant do what all generic applicants must do—prove bioequivalence. As noted above, we made no judgment about the legitimacy of the request in assembling the pool.

The final category of petitions has a less direct link to delaying generic approval. On occasion, pharmaceutical companies do not address specific generic applications or generic approval in general in their citizen petition. Rather, the branded company requests that it be assigned additional exclusivities by the FDA or retain exclusivities that the company perceives to be under threat.\(^83\) We have chosen to categorize these petitions as potentially related to generic delay because gaining exclusivity pushes back the window for generic entry. Adding exclusivity is thus an attempt to extend the current state of the market—in which only a brand-name firm can compete, or only a brand-name firm and a first filer can compete, for example—which for existing sellers is preferable to having a new generic enter the space. Interestingly, one petition filed by a pharmaceutical company openly identifies the relationship between its exclusivity request and delay of competitors: “The requested stay would… prevent the approval of any ANDA or Section 505(b)(2) application referencing the Ziana\(^\text{TM}\) NDA during the 3-year [\textit{sic}] of market exclusivity that would be earned by the Ziana\(^\text{TM}\) application if [the petitioner’s other] citizen petition is granted.”\(^84\)

The final pool of citizen petitions with the potential to delay introduction of generic drugs consisted of 249 citizen petitions filed between 2000 and 2012. Thus, 22% of citizen petitions

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\(^83\) For example, Petition FDA-2010-P-0188 asks the FDA to “confirm,” among other related requests, that “FDA will grant 180-day marketing exclusivity to Actavis’ ANDA No. 77-302.” https://www.regulations.gov/#!documentDetail;D=FDA-2010-P-0188-0001

related in any way to drugs\(^85\) and 14\% of the all citizen petitions filed on any topic at the FDA\(^86\) have the potential to delay the entry of generics.

3. Timing of the Citizen Petitions relative to Generic Applications

For each of the 249 citizen petitions in the data set, we attempted to glean timing data about the petition’s timing relationship with the generic application implicated by the petition. Namely, we wanted to know how much time had passed between when the relevant generic application was submitted and when the citizen petition was filed. We also wanted to track how much time had passed between when the citizen petition was filed and when the generic application was approved. Calculating these statistics required us to have information on when generic applications were filed and approved. One would expect that such information would be readily available in the FDA’s public information, but such is not the case.

a. Filing Dates for Generic Applications

The FDA searchable database contains readily available information on the approval dates for most generic drugs. Filing dates, however, are not so transparent.\(^87\) Assembling

\(^{85}\) That is, 249 of 1158 citizen petitions filed that were related in any way to pharmaceuticals.

\(^{86}\) That is, 249 of 1790 citizen petitions filed on any topic at the FDA.

\(^{87}\) Approval dates are, for the most part, readily available through the FDA’s searchable database of approved drugs, known as Drugs@FDA. See https://www.accessdata.fda.gov/scripts/cder/drugsatfda/For example, anyone can search Drugs@FDA for information on ANDA No. 90153 (a generic version of Ambien CR), and the page clearly denotes an approval date of March 25, 2013. But filing dates are not so transparent. The FDA does not have a standard data field in Drugs@FDA for ANDA filing date — clicking the “Approval History, Letters, Reviews, and Related Documents” link on the page for ANDA No. 90153 results in no history, letters, or documents whatsoever other than another note displaying the approval date for the drug. This was the case for the majority of ANDAs we explored in the Drugs@FDA database. The only way to obtain filing dates is through rarely posted approval documents on a drug’s “Approval History, Letters, Reviews, and Related
information on when a generic application was filed required a combination of sleuthing through the various letters in the generic drug’s public file and estimating based on information known from other drug applications. The process allowed us to determine with reasonable certainty the quarter in which an application for a particular generic application was filed for [X%] of the 249 citizen petitions in our pool.

In particular, the way that numbers are assigned to generic applications makes it possible to estimate filing dates for those generic applications that do not have publicly available approval letters. To do this, however, we needed to look at the full set of all generic applications filed with the FDA between 2006 and the end of 2015, which consists of more than 4,200 applications.\(^{88}\) 2006 was the starting point of our range because we determined that very few drugs approved before this year were implicated in our set of citizen petitions filed between 2000 and 2012.\(^{89}\)

In assembling the data set of generic applications, we included a wealth of information such as the active ingredients, dosage form, generic company, and the name, number, and

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\(^{88}\) We also matched the generic applications to the reference drug using the FDA’s Orange Book data. See text accompanying notes 30-32 (describing the Orange Book).

\(^{89}\) In rare exceptions, we found that citizen petitions in our data set, of 249 petitions between the years 2000 and 2012 with the potential to delay generic competition, related to generic applications that were filed prior to 2006. We were able to use the same techniques described in this section to fill in filing dates for the relevant generic application. Similarly, the FDA database of generic applications does not include approved 505(b)(2) applications. Thus, those applications were added as well, when necessary for the 249 citizen petitions.
company for the original reference drug. We then sorted all of the generic applications by application number. This was a crucial step because generic application numbers are generally assigned sequentially within the different numerical series that exist. For example, generic applications for drugs initially approved before 1962 were assigned numbers in the 80,000s in order of filing date. The 80,000s numbering scheme was replaced by sequential numbering starting in the 40,000s for generic applications referencing post-1962 FDA approvals.

For generic applications referencing drugs approved in the Hatch-Waxman era beginning in the 1980s, numbers were originally assigned in the 70,000s. That numbering scheme was eventually replaced by a 90,000s numbering scheme in late 2007. As explained in the prior paragraph, all 80,000 application numbers refer pre-1962 applications.) The advent of the 90,000s numbering scheme also retired the concurrently-running 40,000 series, so all generic applications from that point on were sequentially numbered in the 90,000s.

When the FDA moved to a new IT platform in mid-2009, numbering changed once again. All drugs, including new drug applications and generic drug applications, were assigned six-digit numbers in the 200,000s. (Before this point, new drug applications were assigned five-digit numbers in the 20,000s, with even lower four- and five-digit numbers earlier in the FDA’s history.) In general, this numbering has remained mostly sequential in order of filing date, but the 200,000 series is riddled with inconsistencies, in part because the FDA has allowed drug companies to reserve filing numbers before full submission of the necessary application materials.

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90 Estimated switch time is based on our database.
91 [http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2012/01/fda-denies-petition-seeking-to-add-application-information-to-drug-labels.html](http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2012/01/fda-denies-petition-seeking-to-add-application-information-to-drug-labels.html). To further complicate the numbering history, Generic applications for antibiotics were previously assigned numbers in the 50,000s and 60,000s. These series were also retired when the 90,000s numbering scheme was introduced.
The FDA’s convoluted numbering history, despite its twists and turns, offers helpful clues about when a drug application was filed. A generic application filed in the 40,000s was filed after one numbered in the 80,000s; a generic application filed in the 70,000s came before an generic applications in the 90,000s; a 200,000s generic application was filed later than any 90,000s generic applications; and so on.

On a more detailed level, sequential numbering within a given numerical series allowed us to estimate filing dates for most generic applications within a quarter-year by using the filing dates the FDA occasionally provides in approval letters. Quarter-years were chosen as the time unit for this paper because they represented the best trade-off between being able to estimate a fair majority of filing dates while also maintaining the level of granularity needed to examine citizen petition timing, where a few months can make a difference in delay. For example, the FDA must respond to citizen petitions filed after mid-2012 in 150 days — between one and two quarters. First-filer exclusivity lasts 180 days—precisely two quarters. Few parts of the generic system, however, work on a weekly or monthly or other level more granular than a quarter-year. When an estimate could not be made properly — for example, if the two available dates bookending an empty generic application were in two separate quarters — no quarter is entered. Again, this was an effort to err on the side of caution in assembling the information.

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92 By quarter-year we mean the following: January-March is in the first quarter of a year, April-June is the second quarter, July-September is the third quarter, and October-December is the fourth quarter. For example, generic application No. 77715 was filed on May 19, 2005 (the second quarter of 2005), and generic application No. 77743 was filed on June 15, 2005 (also in the second quarter). With those two bookends available, we know that all generic applications in between, such as 77725, 77733, and 77741 — all generic applications for which filing dates are not available — were almost certainly also filed in the second quarter of 2005. In our database, we marked these generic applications as having been filed in “2005-2,” with “2” representing the second quarter. A flag was also included to denote which filing dates were estimates and which were actual dates provided by the FDA.
This estimation process should be accurate in the vast majority of cases, but we do note that there may be occasional errors, particularly for generic applications numbered in the 200,000s. Fortunately, few citizen petitions were matched to generic applications in the 200,000 series that had to be estimated. Only 4 citizen petitions that required estimated filing dates were linked to generic applications in the 200,000 series.

Of the roughly 4,000 generic applications approved between 2006 and 2015, 980 had exact filing dates available in approval letters, representing 23%. A further 2,108 filing dates were estimated using the process described above. In all, filing quarter-years were found or estimated for 3,088 generic applications, a success rate of 73%.

b. Matching Citizen Petitions to Relevant Applications

Having constructed the data set of filing and approval dates for generic applications, we then sought to match the data set of approximately 249 citizen petitions with the generic applications implicated by these petitions. In other words, what generic application would be most directly impacted by the filing of the citizen petition?

Occasionally, the “offending” generic application would be explicitly named in the citizen petition. In most cases, however, the object of the citizen petition’s complaint was not so clear, perhaps because drug companies want to spread a wide net over all potential generic applications related to their existing drug. Similar to many citizen petitions, for example, petition FDA-2009-P-0364 states, “Graceway respectfully requests that FDA refuse to approve any

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93 For example, petition FDA-2012-P-0184 specifically asks that the FDA “refuse to accept Cypress ANDA No. 20-2820 for filing (or find ANDA No. 20-2820 not approvable if already accepted for filing).” See https://www.regulations.gov/#!documentDetail;D=FDA-2012-P-0184-0001
ANDA for a generic imiquimod cream product that seeks to rely on FDA’s prior approval of Aldara, unless the application contains data from [bioequivalence studies, among others].”\(^9^4\)

When a specific generic application was not identified, we turned to our generic application data set to find the first generic application filed.\(^9^5\) The first-filer is significant for a number of reasons — it opens the floodgates to generic competition, bringing an initial drop in price and market share and more substantial reductions as other generics enter later on. Thus, the first generic application is the most lucrative milestone for a brand-name company to delay or block.

Making this determination requires careful analysis, given that a drug’s characteristics outside of the active ingredients, such as dosage or route of administration, often mattered in making the first-filer determination. Consider, for example, FDA-2011-P-0702 (filed September 23, 2011). This citizen petition asks the FDA not to approve any generic applications, Doryx (doxycycline hydrate). The petition specifically refers, however, to generic applications “for a 150 mg doxycycline hyclate delayed-release tablet product.”\(^9^6\) Thus, the generic application relevant to the petition is most likely application No. 91052, the first filing for a 150mg delayed-release tablet form of the drug.

Although we generally looked for the first-filed generic application as the appropriate reference point for a citizen petition, in a few instances the first-filer still could not have been the subject of the citizen petition. This occurred, for example, when a generic filed a petition seeking to prevent another generic from entering the market. A market with just two or three players is still a potentially lucrative one, so it is not surprising to see generics also engage in citizen

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\(^9^4\) See https://www.regulations.gov/#!documentDetail;D=FDA-2009-P-0364-0001
\(^9^5\) If multiple ANDAs were explicitly named in a petition, we identified the first-filed petition of those mentioned.
\(^9^6\) https://www.regulations.gov/#!documentDetail;D=FDA-2011-P-0702-0001.
petitioning to keep the number of generics down. In these cases, we attempted to identify the next-filed generic application when possible. Similarly, when the first generic company to file an application was already on the market at the time of citizen petition, meaning it could not be the subject of a petition trying to prevent approval or submission, we also chose a later application as most likely related.

One should also note that citizen petitions could be submitted before the first generic application is filed, a type of pre-emptive strike against any generic submission. For example, FDA-2009-P-0042 requests that the FDA approve no applications for a generic version of Agratroban. The petition was filed on January 30, 2009, but we determined that the first generic application (No. 91665) was not filed until two quarters later. In those cases, the time from filing of the generic application to the citizen petition was negative.

Citizen petitions that could not be definitively linked to a generic application or for which appropriate timing data was not available were removed from our analysis. Finally, we removed citizen petitions mentioning drugs for which no generic was yet on the market, presumably because no application has yet to be approved.

At this conclusion of this process, 166 citizen petitions of the 249 originally identified were linked to a generic application and had data available — either a generic application filing

\[\text{97 We note that it is possible, despite our efforts, that the generic application identified is not necessarily the first-filed generic application. If the actual first-filed generic application was never approved, it would not appear in the FDA’s public records. We do not think this occurrence is particularly likely, but we note that the lack of availability of unapproved generic applications may cause our data to miss applications that suffered the most from delay tactics, such as those that had to be withdrawn or those that were never approved because of issues with generic delay.}\]
date, approval date, or both. This is a success rate of exactly two-thirds, or 66.7%, among the citizen petitions identified as having the potential to delay generic entry. In sum, out of roughly 250 citizen petitions that had been identified as having the potential to delay generic entry, we were able to establish time lines for the generic applications with which they are most likely associated for two-thirds.

c. Establishing Key Metrics

Using our final data set of 166 citizen petitions paired with relevant generic applications, we were able to create the following metrics:

- The number of quarter-years between when a relevant generic application was submitted and when the citizen petition was filed (“Quarters Since Generic Filing”);
- How many quarter-years that had passed between when the Citizen Petition was filed and the final approval of the relevant generic application (“Quarters Before Approval”);
- How long did the generic application take to gain approval from start to finish (its “Total Approval Time”);
- And at what point in the relevant ANDA’s pendency was the citizen petition submitted (the “Percentage Into Pendency”).

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98 In rare circumstances, a filing date was available but not an approval date. This occurred when a drug had only been tentatively approved but was still posted on the FDA’s website with an attached letter.
99 As an example, citizen petition FDA-2007-P-0418 was filed on November 9, 2007, the fourth quarter of 2007. We estimated that its relevant generic application, ANDA No. 78441, was filed in the third quarter of 2006. It was approved on May 14, 2009, the second quarter of 2009. Between the third quarter of 2006 (generic application submission) and the fourth quarter of 2007 (citizen petition filing), five quarter-years had passed, so the value of “Quarters Since Generic Filing” for this citizen petition is “5.” Six quarter-years passed between the fourth quarter of 2007 and the second quarter of 2009 (generic approval), so “Quarters Before Approval” for this petition is “6.” Its “Total Approval Time” is 11 quarter-years, which also
Examining these core metrics will reveal trends of how citizen petitions interact with the generic approval process.

IV. Results

A. Overview

As described in the opening section, the results of the study provide empirical evidence that the citizen petition process at the FDA has now become a key avenue for strategic behavior by pharmaceutical companies to delay entry of generic competition. The following sections describe those results, but the most important findings are the following:

- The FDA’s citizen petition pathway is one of the key pathways involved in the modern generation of generic drug delay, playing a role in various game-playing strategies.
- Citizen petitions from competitor companies have essentially doubled since 2003;
- Citizen petitions from competitor companies occupy a striking amount of the process in recent years. Out of all citizen petitions at the FDA (including tobacco, food, dietary supplements, medical devices, etc.) one-in-five is filed by a competitor company asking the FDA not to approve a generic drug.
- Many citizen petitions from competitor companies appear to be a last-ditch effort to hold off generic competition. In fact, the most common grouping of petitions were those filed half-a-year or less before the generic was approved. This is particularly

happens to be the value obtained when “Quarter Since Generic Filing” and “Quarters Before Approval” are added together. This mathematical shortcut does not work, of course, when the citizen petition was filed before the relevant generic application was submitted. The citizen petition came five quarters into the generic application’s 11-quarter pendency, so the “Percentage Into Approval” is approximately 45.5%.
striking given that the overwhelming majority of citizen petitions are denied.\footnote{See Carrier & Wander, supra note 10, at 249, 274 (finding that the FDA denies 81% of the citizen petitions related to pharmaceuticals).} In other words, the results suggest that many competitor petitions are filed late in the game, as a last ditch effort to hold off competition just a little longer, even though they are unlikely to be successful.

- Congressional reforms enacted in 2007 have not stemmed the tide.

### B. Rise in Citizen Petitions with the potential to delay

#### Chart 1 — All Delay-Related Petitions, By Year

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of Delay-Related Petitions (total = 249)</th>
<th>Percentage of Yearly Total Petitions (total = 1790)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>2</td>
<td>2/47 = 4.3%</td>
</tr>
<tr>
<td>2001</td>
<td>4</td>
<td>4/63 = 6.3%</td>
</tr>
<tr>
<td>2002</td>
<td>5</td>
<td>5/106 = 4.7%</td>
</tr>
<tr>
<td>2003</td>
<td>12</td>
<td>12/120 = 10.0%</td>
</tr>
<tr>
<td>2004</td>
<td>26</td>
<td>26/178 = 14.6%</td>
</tr>
<tr>
<td>2005</td>
<td>15</td>
<td>15/148 = 10.1%</td>
</tr>
<tr>
<td>2006</td>
<td>24</td>
<td>24/184 = 13.0%</td>
</tr>
<tr>
<td>2007</td>
<td>25</td>
<td>25/160 = 15.6%</td>
</tr>
<tr>
<td>2008</td>
<td>23</td>
<td>23/166 = 13.9%</td>
</tr>
<tr>
<td>2009</td>
<td>32</td>
<td>32/171 = 18.7%</td>
</tr>
<tr>
<td>2010</td>
<td>31</td>
<td>31/149 = 20.8%</td>
</tr>
<tr>
<td>2011</td>
<td>22</td>
<td>22/157 = 14.0%</td>
</tr>
<tr>
<td>2012</td>
<td>28</td>
<td>28/141 = 19.9%</td>
</tr>
</tbody>
</table>

A few notes emerge from this chart. First, it is notable just how many citizen petitions seem to have the potential to delay generic entry, with proportions above 20% in 2010 and nearing 20% in other years. That means one-in-five of all citizen petitions — not just those concerning pharmaceuticals — are related in some way to pending generic applications or brand-name exclusivity in those years. In other words, out of all citizen petitions at the FDA (including...
tobacco, food, dietary supplements, medical devices, etc.) one-in-five is filed by a competitor company asking the FDA not to approve a generic drug in some years.

This chart also adds more evidence for the hypothesis made earlier that petitions rose in popularity as a way to delay generics or raise issues about generics starting in 2003 and 2004. Not only did the number of citizen petitions rise noticeably after 2002, but the number of delay-related petitions also has sharply increased as a proportion of all petitions.

**When are Citizen Petitions Filed in Relation to Final Approval?**

We now turn to the results regarding the timing of when competitors file citizen petitions and the implications of that timing. The results obtained in the following analyses suggest two implications: first, many drug companies are filing citizen petitions in a last-ditch effort just months before generic approval; and second, many of these citizen petitions may be the last barrier standing in the way of final generic approval.

We reached these implications in the following manner. For 151 of the 166 citizen petitions in our data set, both a filing date and an approval date were available for the relevant generic applications, allowing us to calculate the average length of time a generic application takes from submission to approval. We will refer to this as the “total approval time.” On average, the total approval time for generic applications in our data set was pending for 16.5 quarter-years, or just over four years.

The histogram below displays the number of generic applications that fell into the defined category; the first bar, for example, corresponds to nine generic applications that were pending for 0-4 quarters (one year).
It is important to note that the generic applications that make up this calculation were those that had related citizen petitions. Thus, the information may not be generalizable to all generic applications. The limitation does, however, allow us to explore whether citizen petition reforms may have had an impact by reducing the total application time for a generic. In particular, despite a 150- or 180-day deadline on responding to citizen petitions, the average total application time for a generic was slightly longer for generics paired with petitions filed post-after the 2007 Amendments. Thus, for generic applications paired with citizen petitions, the total application time was almost 10% longer after the 2007 amendments.¹⁰¹

Next, we graphed the distribution of quarters that passed between filing of the relevant generic application and submission of the linked citizen petition. We refer to this metric as the “quarters since generic filing.” The histogram displays the number of the citizen petitions that fell into each category — for instance, the bar labeled “0-2” indicates that the amount of time

¹⁰¹ Generic applications paired with citizen petitions prior to 2007 had an average total application time of 15.76 quarters compared with 16.95 quarters after the 2007 amendments.
since generic filing was between 0 quarters and two quarters for 19 citizen petitions. This metric was available for 157 citizen petitions.

![Quarters Passed Since Generic Drug Application Submitted and Citizen Petition Filed, 2000-2012](image)

A significant majority — over 75% — of the 157 citizen petitions were filed within 0-14 quarters (0-3.5 years) after the relevant generic application being submitted. More than half were filed more than a full year after the relevant generic application was submitted, indicating that, in general, petitions are not fired off shortly after the announcement of a generic application.

The most interesting and profound result, however, arose when we graphed the amount of time between when a citizen petition was filed and when the linked generic application was approved. We call this metric, “quarters before approval.” Our original hypothesis was that if citizen petitions are being used systematically to delay the approval of generics, citizen petitions might be deployed most effectively near the end of an generic approval cycle. While the generic application approval is in progress, a citizen petition would merely introduce a review process running parallel to the generic submission. If we assume that the FDA has the resources to review a citizen petition and a generic application concurrently, the citizen petition might only add trivial delay to the approval process, similar to a computer being able to process a second
task while not slowing execution of the first job.\textsuperscript{102} Meanwhile, if someone who wishes to keep a

generic off the market is able to estimate that the generic approval process is winding down and

nearing final approval, it would be beneficial to file the citizen petition just as approval is

expected, forcing the FDA to spend months reviewing the claims.

In other words, a “parallel processing” capability is not helpful if the two tasks are not

introduced in parallel; if the second task is introduced only after the first is completed, there can

be no overlap in the performance of the two tasks.\textsuperscript{103} By forcing the FDA to review the petition

at the end of the generic approval timeline, the drug company would stretch out the total time

that a generic application is pending by introducing a last-ditch effort at delay.

The following graph shows the results of this timing inquiry. First, we graphed the
distribution of how many quarters passed between when the citizen petition was filed and when
the generic received approval.

\begin{center}
\includegraphics[width=\textwidth]{graph.png}
\end{center}

\textsuperscript{102} We should not it is not clear whether the FDA truly has this “parallel processing” power,
given ongoing concerns about staffing, mounting backlogs of generic applications, and the
FDA’s own statements about the time-intensive nature of reviewing a citizen petition. Yet, even
if the processing and review is truly not “parallel,” it is reasonable to assume that substantial
parts of reviewing both the generic application and the citizen petition would be completed
concurrently.

\textsuperscript{103} Imagine two tasks, one that will take 2 years to complete and one that will require 1 year to
complete. If both tasks are initiated at the same time, and complete parallel processing is possible
(with unlimited computing power), then both tasks will be finished in 2 years. If the second task
is not started until the first task is complete, the completion of both tasks will still take 3 years
even though the computer or machine has full parallel processing capabilities.
There is a clear trend in favor of citizen petitions filed shortly before the FDA approves a generic. Sixty-one percent of petitions were filed within two years of approval (0-8 quarters), and almost half were filed with just 0-5 quarters to go before generic approval. In fact, the most common category for citizen petitions was “0-2 quarters,” with 45 petitions, or 28% of the total, filed with \textit{half a year or less} remaining before the FDA approved the generic.

In general, the number of petitions filed decreases as the number of quarters between citizen petition filing and generic approval increases. In other words, the trend is towards an increasing number of petitions as one moves closer to the final approval date. Thus, this histogram suggests that generic-related citizen petitions are often filed in the final stages of generic approval to raise last-minute concerns, rather than early or midway through the process. This pattern potentially extends the length of time for, thus delaying the market entry of generic competition.
The following chart looks specifically at the period before the 2007 amendments. In this period, more than 50% of petitions were filed two years or less before approval, with 41% coming 0-5 quarters before approval.

In the period after the 2007 amendments, the trend is particularly dramatic. Sixty-nine percent of petitions were filed within two years of generic approval, and 55% were filed within five quarter-years (0-1.25 years). Most notably, a remarkable 35% of petitions were filed within two quarters of generic approval. The “0-2 quarters” category is by far the most popular, with the second highest category, “3-5 quarters,” garnering 20% of the total.
The biggest exogenous shift between the 2000 to mid-2007 histogram and the mid-2007 to 2012 histogram is, of course, the enactment of the 2007 amendments. Its most notable change may explain why the post 2007 chart paints such a dramatic picture of citizen petition timing. The 180-day timeline for responses to citizen petitions is almost exactly two quarters, or one-half, of a year. From mid-2007 to 2012, we see a plurality of citizen petitions filed within two quarters of final generic approval. In turn, the number of generic approvals coming so shortly after citizen petition filings would indicate that these approvals are coming just as the FDA is disposing, 0-2 quarters later, with the relevant citizen petition. This has two implications: first, many drug companies are filing citizen petitions in a last-ditch effort just months before generic approval; and second, many of these citizen petitions may be the last barrier standing in the way of final generic approval. Anecdotally, this has been the case for some petitions, as evidenced by FDA responses to some requests.

Put another way, when so many generic applications are approved within two quarters — essentially 180 days — of a citizen petition being filed, and the FDA only has 0-180 days to
respond to a citizen petition, the relationship does not seem to be mere coincidence. This may also explain why the trend toward late citizen petitions is not as pronounced in the period before the 2007 amendments: citizen petitions may have still been filed during the late stages of the FDA’s consideration of generic applications, but since the FDA was not held to a specific deadline for responding to citizen petitions, lengthy petition reviews could have pushed back the horizon for final generic approval by more than two quarters or 180 days.

C. When are Citizen Petitions Filed as a Percentage of the Total Application Time?

We consider the results in the section above to be the most significant of the study, but we did discover an additional interesting finding—one that suggests pharmaceutical companies are not following the FDA’s mandate that a citizen petition must be filed as soon as the information comes to light. As described above, the 2007 amendments are intended to encourage those who file citizen petitions to bring the issue to light as soon as they discover it, requiring that filers certify that the petition was not intentionally delayed and provide the date when the filer became aware of the concern.104 The following results suggest that is not the case for our data set of citizen petitions filed by competitors.

Specifically, in tracing timing issues, we focused above on the time between when a citizen petition is filed and the generic is approved, rather than the time between when a generic application is filed and the citizen petition is submitted. Time between filing of the generic application and filing of a citizen petition is not a particularly precise measure of how late a citizen petition is filed, because different applications have different time lengths to approval.

104 See text accompanying notes 57-64, supra.
Just because a petition is filed eight quarters (two years) after a generic application is filed does not mean the petition necessarily came at the midpoint or early stages of the approval process. For example, if the generic petition’s total application time was 10 quarters, the petition would have actually come 80% of the way through the process. Similarly, even if a citizen petition was filed just two quarters before approval, this would not be particularly late if the approval process only spanned four quarters.

However, a more relative look at citizen petition timing can be constructed. We calculated the “Percentage into Pendency” — defined as a standardized measure when the citizen petition was filed as a percentage of the overall generic application approval length.

On average, we find that citizen petitions are filed 56.8% of the way into the pendency of a generic application. In the set of 135 generic application-petition pairs used in this calculation,105 the average pendency was approximately 17.8 quarter-years (~4.45 years), and the average citizen petition was filed 9.1 quarter-years into pendency (~2.28 years). In other words, the average citizen petition came roughly half-way through the petition process.

To illustrate, the histogram below shows the number of citizen petitions grouped into the ten deciles between 0% and 100% percentage into pendency. For example, the first bar represents all citizen petitions that had a percentage into pendency ranging from 0% to 10%.

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105 This calculation was only available if both filing dates and approval dates were available for an generic application, and it was not calculated if the citizen petition was filed before generic application submission, because then the Percentage Into Pendency would be negative, which skews averages and other descriptive statistics. A total of 135 generic application-petition pairs met these criteria, representing 81% of the petitions for which some data was available.
Here, about 55% of petitions were filed more than 50% of the way into pendency, and 37% were filed during the last 30% of pendency. These findings do not differ significantly from a uniform distribution where each decile would contain 10% of citizen petitions, although perhaps more notable is that fewer than three-tenths of petitions were filed during the first 40% of pendency.

The key issue, however, is the following. The 2007 amendments formally require petitioners to declare that the filing was made as soon as the relevant information came to light. Given that the issues mentioned in citizen petitions are often apparent deficiencies in the relevant generic application itself, one might expect to see petitions early in the process, if the system were working properly. Thus, we would not expect petition filings to be evenly distributed during pendency. Nor would we expect to see petitions grouped at the midpoint or later on, in the manner seen in the histogram.
It is also worth noting that the act of filing a citizen petition itself affects the pendency metric. Since a citizen petition can delay generic approval, the citizen petition may extend pendency beyond what would otherwise be expected. The result would be the appearance that the citizen petition surfaced earlier in the approval process than it actually did. This effect may be particularly pronounced in the period before the 2007 amendments, when citizen petitions were not subject to a response deadline and could drag on much longer.

To explore this hypothesis, we once again separated the data into slices before and after the 2007 amendments. No major trend appeared for citizen petitions filed before enactment of the amendments. In this period, the average petition appeared 51.4% of the way into pendency. Only 47% of petitions were filed in the last half of generic application pendency, although the most popular category for filing was in the last tenth of pendency (shared with those filed between 40%-50% of the way through approval).
The findings for the period after the 2007 amendments reveal a stronger trend toward later filing in recent years. This trend perhaps offers some validation for the hypothesis that extended review time for citizen petitions skews pendency data for petitions filed before passage of the 2007 amendments.

The average petition during the period after the 2007 amendments was filed more than 60% of the way into pendency. More than 42% of citizen petitions were filed during the final 30% of generic application approval, and the most common category were those petitions filed 80%-90% through the approval process. Notably, only 13.8% of petitions came during the first 30% of generic application pendency. Thus, it is unlikely to be coincidental that citizen petitions are coming so shortly before generic approval. Nor do the results suggest that competitors filing citizen petitions—many of which claim to have found deficiencies in the generic application—are filing them as soon as the information is uncovered. Finally, the results, taken together, do not suggest that the 2007 amendments have succeeded in ending the practice of filing citizen petitions to delay generic entry.

![Percentage Into Pendency, mid2007-2012 (post-Food and Drug Administration Amendments Act 2007)](chart.png)
D. Did the 2007 Amendments do the Job?

As described above, Congress amended the Food & Drug Administration Act in 2007 in an effort to prevent citizen petitions from being used to delay generic entry. The 2007 amendments require the FDA to respond to citizen petitions concerning generic applications within 180 days (shortened to 150 days in 2012); requires those filing such petitions to certify that the petition was not intentionally delayed and provide the date when the filer became aware of the concern, and gives the FDA the power to summarily deny such petitions in certain circumstances. Our study suggests that those amendments have failed to stem the tide.

Imposing deadlines of 180 days for the FDA to respond and shortening that to 150 days may have reduced the length of the delay, but has by no means deterred the behavior. As detailed above, many competitor petitions continue to be filed late in the game, as a last ditch effort to hold off competition just a little longer, even though they are unlikely to be successful.

In particular, the FDA’s power to summarily dismiss frivolous petitions also appears toothless in application. In its own annual reports, it has mentioned several times that the requirement that the petition both intend to delay generic and raise no valid scientific or regulatory issue is a standard that is “extremely difficult to meet.” In fact, as of fiscal year 2014, the FDA had never denied a petition under this provision.

The 2007 amendments require that the FDA submit an annual report detailing issues related to the 505(q) program created by the amendments. Although providing only aggregate numbers, the report suggests that number of citizen petitions that fall within the 505(q) program

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106 See text accompany notes 57-64, supra.
107 2014 FDA 505(q) report at 9.
108 2014 FDA 505(q) report at 9.
have only increased since passage of the amendments. In 2008, the FDA report shows 21 petitions filed, with that number rising to 28 in 2014. Similarly, the number of petitions handled overall by the FDA’s Center for Drug Evaluation and Research has increased, from 78 in 2008 to 102 in 2014.¹¹⁰ The FDA has further complained about “serial petitioning,” in which the FDA must respond to multiple petitions submitted sequentially about the same drug, a strategy that can delay approval for a considerable amount of time even though the FDA must respond to each petition within 150 days.¹¹¹ One should note, as well, that the definition of 505(q) petitions does not include all petitions that have the potential to delay generic entry.¹¹²

In the report, the FDA must also show how many generic applications were delayed by citizen petitions.¹¹³ On its face, the picture looks quite rosy. Of the relevant citizen petitions that the FDA has resolved in seven years of reporting (2008-2014), only seven petitions technically resulted in delay under the FDA’s definition.¹¹⁴ The problem, however, lies in the definition. First, a citizen petition filed before the relevant generic application is submitted or pending is not subject to 505(q).¹¹⁵ Second, if a generic application is not ready for immediate approval at the time of petition filing, answering the petition within 150 days does not count as “delay,” a scenario that the FDA says is the case in “many instances.”¹¹⁶ Additional important categories of petitions also are not included under 505(q), including petitions that relate to the 6-month

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¹¹⁰ 2014 505(q) report p.7. The numbers of overall drug-related petitions, according to the FDA’s definition, does not include suitability petitions (defined in Part III) and over-the-counter monograph petitions. P.7, footnote 7.
¹¹¹ 2014 505(q) report p. 10
¹¹² See text accompanying notes 115-117, infra; see also Carrier & Wander, supra note 10, at 269.
¹¹⁴ 2014 FDA 505(q) report at 8-9.
¹¹⁶ 2014 FDA 505(q) report at 9.
exclusivity for the first generic filer or petitions about one’s own application.\textsuperscript{117} Painted this way, the citizen petition picture does not look so rosy.

In short, all of the trends we observed were stronger when isolated to the period after the 2007 amendments. Part of this difference is likely due to the fact that the 150- and 180-day response deadlines enacted in the 2007 amendments mean that some petitions are dispensed with more quickly. Thus, the period from citizen petition submission to generic approval is not stretched out as much by petitions as it often was before the 2007 reforms. However, considering we also found that generic application pendency has not decreased since the 2007 amendments — and may have actually increased — it appears that the reforms have not led to a systematic decrease in the length of time to get a generic application to market. Avoiding delay, of course, was the goal of the 2007 amendments. Finally, delay-related petitions have not decreased over time, according to both our own analysis and the FDA’s classification of section 505(q) petitions.

These findings do not mean that Section 505(q) has been totally ineffective. The 150- and 180-day response deadlines for petitions certainly prevents any one citizen petition from extending the generic approval process for a significant amount of time, a huge improvement over the days when petitions could be pending for years.\textsuperscript{118} Nevertheless, while the possible magnitude of abuse may have been curbed, the amount of abuse that is taking place has not seemed to decline. Many petitions are still filed very late in the approval process, the number of petitions has not declined, and there is evidence that petitions are filed even later after passage of the 2007 amendments. If a petition still manages to hamper the FDA for a few months, that delay

\textsuperscript{117} 505(q) guidance p.4, 21 U.S.C. §355(q)(4).
\textsuperscript{118} See Carrier & Wander, supra note X, at 285-286 (detailing a citizen petition process that delayed the introduction of a generic version of the insomnia drug Ambien for more than 3 years at a cost of $3.1 billion).
or slowing of the generic approval process can still be worth hundreds of millions of dollars in unfettered monopoly sales.

While the 2007 amendments may have reduced the length of the delay, they have failed to stop the tactic. As long as the benefits of 5 months of delay (150 days) can be worth hundreds of millions of dollars, companies will be tempted to follow this path, and consumers will continue to pay the price. A different approach is needed.

V. The Road Ahead

As described in the prior section, the citizen petition process has been hijacked as a route for pharmaceutical companies to frustrate generic approvals. We find evidence that many citizen petitions are not filed as soon as potentially worrisome information about a drug is discovered, but instead near the later stages of the generic approval process. Over 60% of potentially delay-related citizen petitions between 2000 and 2012 were filed with two years or less to go until generic approval, with numbers even higher when the data is restricted to the period after the 2007 amendments. In fact, 35% of citizen petitions after the 2007 amendments were filed within two quarter-years of the final approval of the generic drug, suggesting that these petitions were some of the last barriers standing in the way of approval for some generics. Considering citizen petition filings relative to a standardized generic approval time length, we find that the average citizen petition in the period after the 2007 amendments was filed more than 60% of the way through generic application’s pendency, with more than 40% filed during the last three-tenths of pendency.
Also troubling is that citizen petitions appear to be the main catalyst and foundation for attempting many other obstructionist delay strategies. As Feldman and Frondorf have documented, pharmaceutical companies are increasingly focusing their efforts to head off generic competition on obstruction tactics that utilize administrative processes. Such tactics include skirmishes over drug labels and inserts, as well as using a safety program known as REMS to refuse to give generic companies samples of the branded drug necessary for demonstrating bioequivalence in the approval process.\textsuperscript{119} Many of these delay tactics operate through the citizen petition process.\textsuperscript{120} Thus, citizen petitions are no longer simply a tactic to slow down generic entry by suggesting deficiencies in the generic’s application, they are now a primary portal through which pharmaceutical companies attempt to make changes and raise concerns (often spurious) to obstruct or delay generic approval. At the moment, the FDA is powerless to stop it, but what pathways would be more effective?

Looking at the nature of the problem, one could imagine three types of approaches to curb the behavior. These could include 1) a simple prohibition, if one were to conclude that most behavior in the category is likely to be inappropriate; 2) procedural blocks to ensure that the behavior cannot create sub-optimal results; or 3) punitive measures as a deterrent. The section below describes each and sets out mechanisms for accomplishing the goals. The details of the mechanism are less important, however, than choosing among the pathways and identifying the proper incentive structures and the optimal institutional actors.

\textsuperscript{119} For a detailed discussion of these practices, see Feldman & Frondorf, supra note x; see also Hearings on the CREATES Act: Ending Regulatory Abuse, Protecting Consumers, and Ensuring Drug Price Competition, Senate Committee on the Judiciary Subcommittee on Antitrust, Competition Policy, and Consumer Rights, Testimony of Professor Robin Feldman (June 21, 2016) (discussing abuse of the REMS safety protocol process) available at http://www.judiciary.senate.gov/meetings/the-creates-act-ending-regulatory-abuse-protecting-consumers-and-ensuring-drug-price-competition.

\textsuperscript{120} See Feldman & Frondorf, supra note x.
A. A Simple Prohibition

The simplest approach for curbing abuse of the citizen petition process would be to prevent competitors from filing citizen petitions related to generic applications. This would be analogous to the per se rules in antitrust. If one concludes that the vast majority of behavior within a certain category is likely to be improper, societal resources may be better served by declaring the category per se off limits, rather than weighing each instance.

Thus, in the antitrust context, the Supreme Court has noted that

“[t]he rationale for per se rules in part is to avoid a burdensome inquiry into actual market conditions in situations where the likelihood of anticompetitive conduct is so great as to render unjustified the costs of determining whether the particular case at bar involves anticompetitive conduct.”\(^{121}\)

Similarly, one author has described the limitations on patentable subject matter by explaining that, “with certain categories of patents, so few things within that space are likely to survive scrutiny that we cordon off the area for all.”\(^{122}\)

This approach carries a certain cynicism regarding the likelihood that companies would have society’s best interests in mind when commenting on whether the FDA should trust their competitors to enter the market. It is a little like the fox offering to guard the henhouse. The incentives simply are not well-aligned with the desired outcome. Nevertheless, although banning competitors from filing citizen petitions is a simple approach, it is also simplistic. Pharmaceutical companies are likely to argue that, as the actors in the field most familiar with a drug, they are in the best position to sound the alarm when problems are on the horizon. Nor

\(^{122}\) Feldman, supra note x, at 99 (describing the limitations on patentable subject matter in patent law and noting that “with certain categories of patents, so few things within that space are likely to survive scrutiny that we cordon off the area for all.”)
would the approach necessarily be fully effective. Companies could still submit generalized citizen petitions before any generic applications are filed or file petitions related to the drug that have the effect of delaying entry—for example, by asking the FDA to reconsider all labeling related to the drug—without requesting such delay.

B. Procedural Blocks

An alternative approach would involve enacting procedural blocks to channel the behavior into positive, rather than suboptimal results. Thus, one might wish to preserve the citizen petition process for all—including competitors—and yet ensure that citizen petitions filed by competitors do not delay generic entry.

For example, one might direct that citizen petitions filed by competitors must be filed within a year of when the generic company files for approval.\footnote{123} Given that the average length of time for a generic application is 4 years, citizen petitions filed within a year are less likely to delay final approval.

Similarly, when competitors raise an issue related to the drug in general, the rule could be that the generic application goes forward on a timeline unrelated to the citizen petition. In other words, the generic can receive approval, and whatever issue is raised can be resolved after that approval, if necessary. After all, the branded drug remains on the market under the current requirements for the drug, which suggests that the issues raised in the citizen petition are not of such magnitude that the drug cannot be offered to the public. Thus, whatever issues must be resolved, would be resolved as to all forms of the drug—generic and brand-name—on a timeline unrelated to the generic’s approval. One could refer to this as the “band plays on” rule.

\footnote{123}{This would require that the FDA make all generic applications public and easily searchable when they are filed.}
Societal resources are still at risk. The FDA must spend time responding to each concern raised. Similarly, branded companies could still use the behavior to raise their rival’s costs. In other words, generic competitors conceivably could be forced to spend time and money responding to spurious issues raised. Nevertheless, with the prospect of delayed entry off the table, such a procedural block could substantially a brand-name company’s incentives to engage in this behavior. Of the choices discussed here, this may, indeed, be the most effective.

C. Punitive Deterrents

The third approach would incorporate some form of punitive measure designed to deter abuse of the citizen petition process, either through the courts or the FDA. Thus, parties that engage in behavior to try to block or delay generic entry through citizen petitions could be subject to a penalty calibrated to deter any but the hardiest of souls from engaging in the behavior in the first place.

In contemplating this approach, the initial question would involve determining the proper adjudicatory body to decide whether the behavior falls beyond bounds. In theory, one might suggest that the FDA is the proper adjudicatory body. After all, the Agency has the greatest expertise for evaluating whether the issues raised in a citizen petition are spurious or well-founded.

The FDA, however, has proven more effective at evaluating patient safety than party behavior. The Agency has had the power since 2007 to summarily deny any petition filed with the primary purpose of delaying generic approval if the petition does not also raise valid

124 See Thomas G. Krattenmaker & Steven C. Salop, Anticompetitive Exclusion: Raising Rivals’ Costs to Achieve Power Over Price, 96 YALE L.J. 209 (1986) (seminal work identifying ability of competitors to impose costs on rivals without similarly incurring such costs).
scientific or regulatory issues.\textsuperscript{125} As noted above, the FDA had not used the provision even once through fiscal year 2014. It is certainly possible that a differently worded authority would prompt greater activity from the Agency. Nevertheless, one could argue that such a role may not be the right fit. The FDA may be better suited for evaluating scientific bad behavior than competition bad behavior.

An alternative would be to provide greater power for competition authorities (such as the FTC or the DOJ) or third party actors (such as the competitors who suffer harm) to act against anticompetitive behavior involving citizen petitions. In general, however, antitrust actions such are slow and expensive.\textsuperscript{126} Moreover, if the experience with pay-for-delay settlements is a guide, by the time the courts slowly begin choking off the behavior, pharmaceutical companies will have altered the tactics.\textsuperscript{127} Antitrust law simply may not be sufficiently nimble.

Most important, providing an effective antitrust pathway for challenging citizen petitions will require substantial shifts in doctrines related to antitrust and regulatory agencies. The \textit{Noerr-Pennington} line of cases, dating back to the 1960s, establishes the general principle that one has the right to petition government without fear of antitrust liability. Although antitrust liability may still attach if one’s petition to the government is judged to be a “sham” the bar for establishing a sham petition is extremely high.\textsuperscript{128}

Certain types of citizen petition actions could be even more difficult to attack under antitrust law. For example, if citizen petitions are used as part of a tactic to prevent a generic

\textsuperscript{127} See Feldman & Frondorf, \textit{supra} note X.
hopeful from obtaining samples of the branded product to demonstrate bioequivalence, antitrust actors trying to challenge the behavior would also run up against Trinko. In the Trinko opinion, the Supreme Court all but shut the door on antitrust actions that claim one’s competitor has improperly refused to sell to you. In general, competitors are not required to sell to each other, and as the Department of Justice has argued, refusals to deal or “forced sharing” rarely helps consumers in the long run. Although providing samples for generic approval may be the rare exception to the rule, getting past Trinko would be difficult, indeed.

In short, Congress or the Supreme Court would have to be willing to alter antitrust doctrines like these in a manner sufficient to allow antitrust actors to bring successful litigation—without, of course, breaking the bank in the process. A punitive measure that costs exorbitant amounts to unleash, will have very little deterrent bite.

D. Transparency

No approach is perfect or a permanent solution. In reality, fixing citizen petitions may require a combination of these approaches. Moreover, recent history has shown that when one the legal system closes off one pathway, pharmaceutical companies will search for others. Thus, whatever paths and approaches are chosen to curb citizen petition abuse, it will be critical to

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ensure that regulators, legislators, and the courts can see new techniques as they emerge. A little sunshine goes a long way.

In particular, greater transparency from the FDA could be tremendously effective in exposing schemes early on. Although the FDA makes a wealth of information publicly available, there are significant gaps in the system. For example, as described in the methodology section, there is no systematic method for finding the date on which a generic application was filed. One could argue that all generic applications should be posted when filed, along with the date of their filing, and that the public should not have to wait until the generic is approved. As it stands now, the more effective one is at blocking generic competition, the longer one has before the public can see what is being done.

At the very least, however, once a generic application has been approved, the public should be able to tell at a glance when the application was filed. Specifically, all approval letters should be on the FDA website, and the FDA website should always list submission and approval dates for every generic – online and not just in letters.

In fact, the FDA appears to be moving in the opposite direction. For our study, we were able to extract filing dates from some of the approval letters that the FDA posted and back fill many others when the FDA approval letters did not mention the filing date. The FDA recently changed its protocols, however, so that the public will no longer be able to do even that. According to one report, the FDA has initiated a new protocol in which it will omit from approval letters any mention of the filing date of the original generic application.131

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Other basic information could improve transparency as well, including more complete labeling of citizen petitions themselves, and full information on generic applications numbers and how they are assigned. Finally, the massive Freedom of Information Act (FOIA) backlog at the agency also operates to shade improper behavior. When we inquired for our research, agency personal were wonderfully helpful but noted that FOIA requests are taking approximately 2 years for a response.

Making full data on generic applications quickly and clearly available to the public is essential for curbing inappropriate behavior. Particularly if the FDA is not assigned the full task of policing competition, others actors—including state and federal regulators, legislators, academic researchers, public interest groups, and generics themselves—must have quick and clear access to the relevant information. Transparency efforts such as these, along with the types of approaches described above for curbing attempts to delay generic competition through citizen petitions, are essential for addressing the problems. Without such endeavors, we will continue to see a citizen’s process diverted to the service of pharmaceutical companies playing games to hold off generic entry as long as possible. Consumers, of course, pay the price.