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**Patent Law:**  
*Empirical Evidence of Drug Pricing Games—  
A Citizen's Pathway Gone Astray*

Robin Feldman<sup>1</sup>

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 Food and Drug Administration (FDA) estimates that consumers saved \$254 billion in 2014 through generic competition and achieved a total of \$1.68 trillion of savings in the decade between 2005 and 2014. 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. After generic competition begins, the price of most drugs eventually falls to 80% to 85% below the original brand-name cost.

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." It is also not surprising that patent holders try to prevent falling into the approaching chasm using any means possible. 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

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1. Summarized and excerpted from Robin Feldman et al., *Empirical Evidence of Drug Pricing Games—A Citizen's Pathway Gone Astray*, 20 STAN. TECH. L. REV. 39 (2017). For more information visit the website at <https://law.stanford.edu/stanford-technology-law-review-stlr/>. In accordance with the protocols outlined in the *Harvard Journal of Law & Technology Open Letter on Ethical Norms*, all of the data is publicly available for future use by other academics on SSRN.com. See Robin Feldman et al., *Database from Empirical Evidence of Drug Pricing Games—A Citizen's Pathway Gone Astray*, SSRN (Mar. 7, 2017) [https://papers.ssrn.com/sol3/papers.cfm?abstract\\_id=2924673](https://papers.ssrn.com/sol3/papers.cfm?abstract_id=2924673) [<http://perma.cc/B8S4-PEYH>]. In further accord with the *Open Letter*, the University of California Hastings Institute for Innovation Law, which Robin Feldman directs, has made donation information available. See <http://innovation.uchastings.edu/about/funding/funding-for-academic-year-2015-2016> [<http://perma.cc/EK2K-XB72>]. No private or corporate donor accounts for more than 10% of the Institute's budget.

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 them. Even if these tactics are likely to fail in constructing a permanent generic blockade, they are relatively costless and easy to attempt; and even if they only secure a few months of last-ditch delay, those precious few months 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, slowing submersion, even marginally, can be extremely valuable.

With anecdotes as well as recent scholarship, concerns have swirled around the citizen petition process at the FDA. The FDA's citizen petition process was created in the 1970s, along with similar programs at other agencies, and was intended 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 designed to police. Recent evidence suggests, however, that the FDA's citizen petition process may have taken a different turn. That issue is analyzed here.

The citizen petition process was mandated by Congress's passage of the Administrative Procedure Act, which requires federal agencies to create a formal route for the public to petition an 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 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 its concerns to a key regulatory agency. A mechanism designed for concerned citizens and scientists to raise concerns 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.

As an example of a troubling citizen petition, consider the petition filed in 2007 by Mutual Pharmaceuticals, a company the FDA had already approved to sell a generic version of the blood pressure medicine felodipine. 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. The petition further suggested that all new generic drug approvals should be delayed until the FDA asked the original drug maker to specify which form of orange juice was used in its studies. Of course, as a currently approved seller of generic felodipine, the company writing the citizen petition would be free to continue selling the existing labels based on 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. Seville oranges are a smaller, more bitter orange often used for marmalade and liqueurs. The FDA, however, was unimpressed. 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.” In fact, the FDA seemed 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.

A footnote hinted at the FDA's skepticism of 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 (i.e., the 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. Mylan, a competing generic-drug company, filed the next generic application in the first quarter of 2007, just months before Mutual filed 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 by delaying the approval of a second generic for felodipine.

This example of felodipine fits the rumors swirling about the current modus operandi for citizen petitions—pharmaceutical companies make a facially interesting, scientific-sounding claim (for example, Seville orange juice actually *does* increase absorption and peak drug concentration) timed to the months right before generic application approval, and the claims are eventually denied by the FDA. Despite the eventual denial, the delays cost consumers untold sums and waste governmental resources.

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 thirty-year history. These changes attempted to address concerns with citizen petitioning at the FDA, ranging from growing petition backlogs to signs that the process was being used inappropriately to delay entry of generic drugs. The Amendments aimed to curb attempts to both block and delay the entry of generics.

Specifically, the 2007 Amendments added subsection "(q)" to 21 U.S.C. § 355, 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."

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 further shortened to 150 days through the Food and Drug Administration Safety and Innovation Act (FDASIA). Approval of a generic application cannot be delayed because of a citizen petition beyond the 180-day (and later 150-day) review period, unless it is determined that a delay is necessary for public-health reasons.

Most importantly, § 505(q) contains provisions intended to deter those who would file citizen petitions to delay generic competition. If a citizen petition relating to a generic application falls under § 505(q), the person filing the petition must certify that the petition is not frivolous, all information favorable and unfavorable has been provided, and the petitioner did not intentionally delay filing the petition. 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) grants 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 face raise valid scientific or regulatory issues.” Together, the provisions of § 505(q) were meant to end 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 the data, allowing observations of 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 exploration.

As described above, anecdotes have swirled for years suggesting that drug companies abuse the citizen petition process to keep generics off the market. The goal of the quantitative look taken here was to empirically explore whether pharmaceutical companies systematically use the citizen petition process to delay entry of generic drugs.

Exploring that question, required an analysis of the timing of when citizen petitions were filed during the generic drug approval process and the frequency with which petitions that have the potential to delay were filed. The hypothesis was that such petitions had been filed towards the end of the approval process to put up one more roadblock in the path of successful approval of a generic drug.

Assembling the necessary information from the FDA’s publicly available files was tremendously difficult. Although the FDA publishes a large amount of information on its public website, and more in hard copy through its Orange Book, much important information is absent. The necessary information often must be pieced together or estimated; in some cases, it simply cannot be located. For example, the FDA does not

always publicly reveal the dates when generic applications are filed. Many of those dates were tracked down by reading PDFs of various letters in the files of approved applications. For many others, however, a method had to be developed for identifying the likely quarter in which an application was filed by working from the FDA's file numbering systems. Despite these challenges, a data set was assembled of citizen petitions that had the potential to delay generic applications, along with the relevant generic application and timing data.

The 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—brand names and generics seeking to delay competitors—have essentially doubled since 2003.
- Citizen petitions with the potential to delay generic entry have constituted a striking portion of the citizen petitions in recent years. Out of all citizen petitions filed at the FDA between 2000 and 2012 (including those concerning tobacco, food, dietary supplements, medical devices, etc.), nearly 15% had the potential to delay a generic drug application, climbing to 20% in some years.
- Many citizen petitions appear to be a last-ditch effort to hold off generic competition. In fact, the most common category of all generic-related petitions was petitions filed within six months of generic approval. This is particularly striking given other research showing that the overwhelming majority of citizen petitions are denied. In other words, the results suggest that many competitor petitions are filed late in the game as a final 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 of such delay-related petitions.

With these empirical findings as a backdrop, three approaches to curb the behavior are possible: (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 suboptimal results; and (3) punitive measures as a deterrent. The data also suggest the need for improvement in FDA data collection and transparency.