

CITIZEN PETITIONS: AN EMPIRICAL STUDY

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ABSTRACT

In recent years, brand-name drug companies have engaged in an array of conduct that has delayed generic competition. While some of the activity—such as settlements between brand and generic firms and “product hopping” from one drug version to another—has received attention, another behavior has, until now, flown under the radar.

This Article examines the activity of “citizen petitions.” A citizen petition is a request for the U.S. Food and Drug Administration (FDA) to take an action such as evaluating a drug’s safety or effectiveness. When used appropriately, it could raise awareness of legitimate concerns with a drug. But when used inappropriately, it could extend the brand firm’s monopoly by delaying FDA approval of generic drugs. This delay could result in literally millions of dollars a day being transferred from consumers to drug companies.

Despite their delaying potential, citizen petitions have not been examined in significant detail. This Article offers the first empirical study of citizen petitions, reviewing every petition filed with the FDA between 2001 and 2010. It finds that petitions have increased in the past decade and that 68% of petitions are filed by brand companies, with more than 75% of brand petitions targeting generic drugs.

The study concludes that the FDA has granted 19% of citizen petitions and has denied 81%. It finds that generics’ petitions are more successful, with 28% granted and 72% denied, as compared to brands’ petitions, of which 19% are granted and 81% denied.

To reduce delays from petitions, Congress enacted legislation in 2007 that required the FDA to rule on certain petitions within 180 days. This study finds that this legislation has not been successful in reducing the number of petitions. After passage of the legislation, the average number of filings per year increased from 27 to 34. Brand petitions against generics increased from 9 to 16 per year. And the grant rate for brands’

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petitions against generics declined from 20% to 19%.

Building on the empirical study, the Article highlights the incentives brand firms have to file petitions, along with the role petitions play in the toolbox of delaying conduct. It also introduces examples that demonstrate the problem, such as the petitions delaying (1) depression drug Wellbutrin for 133 days at a cost to consumers of \$600 million and (2) insomnia drug Ambien for 1225 days at a cost of \$3.1 billion.

The landscape in the pharmaceutical industry today is ripe for petitions, with an impending “patent cliff,” declining drug-company profits, and increased use of related conduct such as brand-generic settlements and product hopping. As a tool that is being used more frequently and that has evaded attempts to limit its abusive potential, citizen petitions warrant scrutiny.

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INTRODUCTION

Some of the most challenging issues presented by intellectual property and antitrust law today occur in the pharmaceutical industry. The industry is characterized by significant regulation, a heavy reliance on patents, and dramatic effects of generic entry. Particularly as the end of the patent term approaches, these characteristics encourage brand-name drug companies to take actions that delay the entry of generic drugs.

Various tools that brand firms have used to delay competition have received widespread attention. One example involves settlements by which brands pay generics to settle patent litigation and delay entering the market. Another involves “product hopping,” or modest changes to drugs with patents about to expire to forestall generic competition. But one potentially delaying activity, involving government petitions, has—until now—flown under the radar.

This Article examines the activity of “citizen petitions.” A citizen petition is a request for the U.S. Food and Drug Administration (FDA) to take a particular action, such as evaluating a drug’s safety or efficacy. When used appropriately, it could raise awareness of legitimate concerns with a drug. But when used inappropriately, it could extend the brand firm’s monopoly by delaying FDA approval of generic drugs. This delay could result in the transfer of millions of dollars per day from consumers to drug companies.

In the past several years, concerns about citizen petitions have received periodic attention. In 2006, the Senate Special Committee on Aging held hearings in which government and industry officials lamented the lengthy delays in the process. In response to the hearing, and as a result of congressional legislation, in 2007 the FDA changed its rules on petitions, promising to respond within 180 days. But despite this attempted solution, citizen petitions continue to delay generic entry.

This Article presents the findings of the first empirical study ever undertaken of citizen petitions. It analyzes every petition filed with the

FDA from 2001 to 2010 and documents (1) how many petitions are filed each year, (2) who files the petitions, (3) who are the targets of the petitions, and (4) the success rate of the petitions.

The study finds that citizen petitions present as much concern as they ever have. More petitions are filed today than were filed a decade ago. In fact, more petitions were filed after the 2007 legislation, which was enacted specifically to limit delay. The study finds that brand drug companies file 68% of petitions, far more than generic firms or other parties such as universities, doctors, or hospitals. Of the petitions by brand firms, more than 75% target generic entrants.

The study concludes that the FDA has granted 19% of petitions and has denied 81%. It also observes that generics' petitions are more successful, with 28% granted and 72% denied, as compared to brands' petitions, with 19% granted and 81% denied.¹ The study finds that brands are more successful filing petitions against other brands (37% granted, 63% denied) than against generics (20% granted, 80% denied).

The study also finds that Congress's 2007 legislation has not been successful in reducing the number of petitions. After passage of the legislation, the number of filings per year increased from 27 to 34. Brand petitions against generics increased from 9 to 16 per year. And the grant rate for brands' petitions against generics declined from 20% to 19%.

Explaining the prevalence of petitions despite the high rates of denial, the Article hypothesizes that many petitions are filed to delay generic entry. Brand firms have significant incentives to file petitions for this purpose, and the activity fits comfortably in the toolbox of activity delaying generic competition, complementing settlements with generics and product hopping.

The Article also discusses examples that demonstrate the problem. In the first, brand company Biovail filed a petition that delayed a generic version of depression drug Wellbutrin XL for 133 days at a cost to consumers of \$600 million. In the second example, Sanofi-Aventis filed a petition that delayed a generic version of insomnia drug Ambien for 1225 days at a cost of \$3.1 billion.

Part I of this Article provides an overview of potentially anticompetitive conduct in the pharmaceutical industry. It introduces the Hatch-Waxman Act, enacted by Congress in 1984 to create a framework for brand and generic pharmaceutical competition. It also discusses settlements between brand and generic firms that delay entry, as well as "product hopping," by which a brand company switches from one version of a drug (for example, tablet form) to another (such as capsule form). It pays particular attention to the importance of generic competition and timing of generic entry.

Part II turns to citizen petitions, specifying the categories, filers,

¹ Third-party petitions were least successful of all, with 0% granted and 100% denied.

and requirements of petitions. It also raises some concerns about these petitions that government officials have articulated. Finally, this Part introduces the 2007 amendment designed to reduce abuse.

Part III presents the results of the first empirical study of citizen petitions. It tracks petitions filed with the FDA from 2001 to 2010, and documents the number of petitions and success rate of the petitions. Most generally, this Part finds that petitions have increased in the past decade and that the vast majority are denied.

Part IV points to one potential reason that so many petitions have been denied: they are filed not because of actual concerns about a drug's safety or efficacy, but because they can delay generic competition. According to this hypothesis, brand firms have significant incentives to file the petitions, which complement settlements and product hopping in prolonging market monopoly. Part IV also discusses the unsuccessful effect the 2007 amendment has had in reducing the number of citizen petitions.

Part V introduces three examples that demonstrate harm from citizen petitions. It shows how petitions filed against Wellbutrin, Ambien, and pain reliever OxyContin delayed generic entry and cost consumers billions of dollars.

The Conclusion recognizes the prominent role played by citizen petitions in brand firms' toolkit in delaying generic competition. Given the landscape in the pharmaceutical industry today—with an impending “patent cliff” and declining drug-company profits—the trend of more (and still questionable) citizen petitions shows no signs of abating.

I. PHARMACEUTICAL COMPETITION

The pharmaceutical industry presents some of the most challenging and important issues in intellectual property, antitrust, and regulatory law today. The regulatory structure governing pharmaceutical competition is the Hatch-Waxman Act. The legislation increased the importance of generic drugs. But as revealed by settlements and product hopping, brand firms have engaged in an array of activity designed to forestall generic competition.

A. *Hatch-Waxman Act*

Congress enacted the Hatch-Waxman Act in 1984 to increase generic competition and foster innovation in the pharmaceutical

industry.²

One central goal of the Act was to promote generic competition.³ Generic drugs have the same active ingredients, dosage, administration, performance, and safety as patented brand drugs.⁴ Despite the equivalence, generic manufacturers were required, at the time of the Act, to engage in lengthy and expensive trials to demonstrate safety and effectiveness. The FDA approval process took several years, and because the required tests constituted infringement of the brand company's patent covering the drug, generics could not begin the process during the patent term.⁵ They therefore waited until the end of the term to begin these activities, which prevented them from entering the market until two or three years after the patent's expiration. At the time Congress enacted Hatch-Waxman, there were no generic equivalents for roughly 150 drugs whose patent term had lapsed.⁶

Congress employed several mechanisms in the Act to promote generic competition. First, the Act allowed generics to experiment on drugs during their patent terms.⁷ Second, the Act created a new process for obtaining FDA approval. It recognized a new type of drug application, called an Abbreviated New Drug Application (ANDA), that allowed generics to rely on brands' safety and efficacy studies, dispensing with the need for generics to conduct their own lengthy and expensive studies.⁸

Finally, and most relevant to concerns presented today, the Act granted 180 days of marketing exclusivity to the first generic to challenge a brand firm's patent or claim that it did not infringe the patent. Such exclusivity was reserved for the first generic firm—known as a “Paragraph IV filer”—that sought to enter during the patent term.⁹ During that 180-day period, which begins after the first commercial

² Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman Act), Pub. L. No. 98-417, 98 Stat. 1585 (codified as amended at 21 U.S.C. § 355 (2006)).

³ For a more comprehensive discussion of the material in this section, see Michael A. Carrier, *Unsettling Drug Patent Settlements: A Framework for Presumptive Illegality*, 108 MICH. L. REV. 37, 41–45 (2009).

⁴ *Understanding Generic Drugs*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingGenericDrugs/default.htm> (last updated July 16, 2012).

⁵ CONG. BUDGET OFFICE, HOW INCREASED COMPETITION FROM GENERIC DRUGS HAS AFFECTED PRICES AND RETURNS IN THE PHARMACEUTICAL INDUSTRY 38 (1998), *available at* <http://www.cbo.gov/ftpdocs/6xx/doc655/pharm.pdf> [hereinafter CBO STUDY].

⁶ H.R. REP. NO. 98-857, tit. 1, at 17 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647, 2650.

⁷ 35 U.S.C. § 271(e)(1) (2012) (exempting from infringement the manufacture, use, or sale of a patented invention for uses “reasonably related to the development and submission of information under a Federal law” regulating the manufacture, use, or sale of drugs).

⁸ FED. TRADE COMM’N, GENERIC DRUG ENTRY PRIOR TO PATENT EXPIRATION: AN FTC STUDY 5 (2002), *available at* <http://www.ftc.gov/os/2002/07/genericdrugstudy.pdf> [hereinafter GENERIC DRUG STUDY].

⁹ 21 U.S.C. § 355(j)(5)(B)(iv) (2006). Three other patent certifications apply in cases where the drug is not patented, the patent has expired, or the generic agrees it will not seek approval until the patent expires. *Id.* § 355(j)(2)(A)(vii).

marketing of the drug, the FDA cannot approve other ANDAs for the same product.¹⁰

B. Generic Entry

The Hatch-Waxman Act has been successful in increasing generic entry. Generic drugs, which made up 19% of prescriptions for drug products in 1984,¹¹ increased to 78% in 2010.¹² For the most popular drugs with expired patents, the share facing generic competition burgeoned from 35% in 1983 to almost 100% today.¹³

Generic entry is a pivotal event in a drug's lifecycle. When generics enter a market, they dramatically lower price. The first generic entrant prices its product, on average, 5 to 25% lower than the brand drug.¹⁴ The presence of a second generic lowers the price to approximately half the brand price.¹⁵ In markets in which six or more generics enter, the price falls to a quarter of the brand price.¹⁶ One survey showed that patients could save 52% in the daily costs of their medications by purchasing generic drugs.¹⁷

In addition, generic drugs quickly take sales from brand drugs. Once a generic enters the market, a brand loses 45 to 90% of its market share within the first twelve months.¹⁸ Generic entry is most likely for

¹⁰ GENERIC DRUG STUDY, *supra* note 8, at 7. Until amended in 2003, the Hatch-Waxman Act provided that a court decision finding invalidity or lack of infringement constituted a second trigger for the 180-day period. See Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub. L. No. 108-173, § 1101(c), 117 Stat. 2066.

¹¹ See *Examining Issues Related to Competition in the Pharmaceutical Marketplace: A Review of the FTC Report, Generic Drug Entry Prior to Patent Expiration: Hearing Before the Subcomm. on Health of the H. Comm. on Energy and Commerce*, 107th Cong. 127 (2002), available at <http://www.gphaonline.org/resources/2002/10/08/greater-access-affordable-pharmaceuticals-act> (statement of Kathleen D. Jaeger, President & CEO, Generic Pharmaceutical Association).

¹² IMS INST. FOR HEALTHCARE INFORMATICS, THE USE OF MEDICINES IN THE UNITED STATES: REVIEW OF 2010, at 22 (2011), available at http://www.imshealth.com/imshealth/Global/Content/IMS%20Institute/Documents/IHII_UseOfMed_report%20.pdf.

¹³ CBO STUDY, *supra* note 5, at 37.

¹⁴ *Id.* at xiii; *Generic Competition and Drug Prices*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm129385.htm> (last updated Mar. 1, 2010).

¹⁵ *Id.*

¹⁶ *Id.*

¹⁷ *Savings From Generic Drugs Purchased at Retail Pharmacies*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/Drugs/EmergencyPreparedness/BioterrorismandDrugPreparedness/ucm134205.htm> (last updated June 26, 2009).

¹⁸ FED. TRADE COMM'N, PAY-FOR-DELAY: HOW DRUG COMPANY PAYOFFS COST CONSUMERS MILLIONS 8 (2010), available at <http://www.ftc.gov/os/2010/01/100112payfordelayrpt.pdf>; CBO STUDY, *supra* note 5, at xiii; DOUG LONG, IMS HEALTH, 2003 YEAR IN REVIEW: TRENDS, ISSUES, FORECASTS 35 (2004), available at <http://www.piapr.org/index.php?src=documents&srctype=download&id=38>; Atanu Saha et al., *Generic Competition in the U.S.*

drugs with large markets, particularly those with blockbuster products, but occurs with respect to drugs in markets of many sizes.¹⁹

These trends are amplified by health plans' encouragement or requirement of generic drugs.²⁰ Most states allow pharmacists that receive prescriptions for brand drugs to substitute generics.²¹ Medicaid policies and managed-care plans also encourage substitution.²²

For these reasons, it is in the brand firms' interests to delay generic entry. Every day a brand firm can control the market and forestall entry is a day it could potentially gain monopoly profits. In the Hatch-Waxman setting, this is particularly tempting since brands could face generic entry before the end of the patent term. For these reasons, brand firms have used an array of tactics to delay entry. The first type involves settlements in which brands pay generics to refrain from entering the market.

C. Brand-Generic Settlements²³

The pivotal effects of generic entry explain the multitude of settlements between brand firms and first-filing generics today. By paying the first-filer to delay entering the market, the brand firm can prevent entry not only by that generic, but also by all other generics. The reason is that these firms cannot enter the market until 180 days after the first filer's entry.²⁴ And as a result of settling with the brand firm, the generic's entry often is delayed for years.

It is in the interests of the brand firm and the first-filing generic to settle, especially with payments from the brand to the generic known as "reverse payments."²⁵ The brand firm benefits by blocking challenges that could invalidate its patent. And the generic receives a subset of the brand's monopoly profits that may even exceed what it could have

Pharmaceutical Industry, 13 INT'L J. ECON. BUS. 15, 31 (2006).

¹⁹ Fiona M. Scott Morton, *Barriers to Entry, Brand Advertising, and Generic Entry in the U.S. Pharmaceutical Industry*, 18 INT'L J. INDUS. ORG. 1085, 1102 (2000); Saha, *supra* note 18, at 27.

²⁰ Alden F. Abbott & Suzanne T. Michel, *The Right Balance of Competition Policy and Intellectual Property Law: A Perspective on Settlements of Pharmaceutical Patent Litigation*, 46 IDEA 1, 23 (2005).

²¹ *Id.* at 23–24.

²² See *In re Schering-Plough Corp.*, 136 F.T.C. 956, 985 (2003), *vacated*, *Schering-Plough Corp. v. FTC*, 402 F.3d 1056, 1058 (11th Cir. 2005).

²³ Material in this section is adapted from Michael A. Carrier, *A Real-World Analysis of Pharmaceutical Settlements: The Missing Dimension of Product Hopping*, 62 FLA. L. REV. 1009, 1014–15 (2010).

²⁴ See 21 U.S.C. § 355(j)(5)(B)(iv) (2006).

²⁵ These are called reverse-payment settlements because they refer to agreements in which payments flow from patentees to challengers, unlike typical agreements in which licensing payments flow from challengers to patentees.

gained through successful litigation and market entry.²⁶ Consumers, on the other hand, could suffer from the elimination of challenges to patents that often are invalid.²⁷

D. *Product Hopping*

Another type of activity in the pharmaceutical industry that has raised the concern of delayed generic entry is “product hopping.” This activity refers to a brand firm’s reformulation of its product, often as a patent is about to expire. Some companies, for instance, switch from a capsule to a tablet (or vice versa), or from either of these forms to an extended-release drug or chewable tablet.²⁸ Much of this product-hopping activity has been successful because it has avoided the effect of state drug product substitution (DPS) laws.²⁹

State DPS laws, which are in effect in all 50 states today, are designed to lower prices for consumers. These laws allow (and sometimes require) pharmacists—absent a doctor’s contrary instructions—to substitute generic versions of brand-name prescriptions.³⁰

DPS laws are designed to address the disconnect in the industry between prescribing doctors (who are not directly responsive to drug pricing) and paying insurers and consumers (who do not directly select the prescribed drug).³¹ In particular, they carve out a role for pharmacists, who are more sensitive to price than doctors.³²

These laws, however, can be evaded when brand firms engage in product hopping. Switching to a new version of the drug prevents a pharmacist from substituting a generic version because the generic is

²⁶ See Carrier, *supra* note 3, at 73.

²⁷ In a study of Paragraph IV challenges between 1992 and 2000, the FTC found that the generic prevailed in 73% of the cases and that the brand firms won only 27% of the time. GENERIC DRUG STUDY, *supra* note 8, at 10, 16. These figures are consistent with a survey of Federal Circuit decisions from 2002 through 2004, which found that pharmaceutical patentees were successful on the merits in 30% of the cases. Paul M. Janicke & LiLan Ren, *Who Wins Patent Infringement Cases?*, 34 AIPLA Q.J. 1, 20 (2006).

²⁸ Keith B. Leffler et al., *Anticompetitive Product Changes in the Pharmaceutical Industry*, 41 RUTGERS L.J. 1, 3 (2010).

²⁹ See *id.* at 13–18.

³⁰ See Carrier, *supra* note 23, at 1017.

³¹ BUREAU OF CONSUMER PROT., DRUG PRODUCT SELECTION: STAFF REPORT TO THE FTC 2–3 (1979), available at <http://babel.hathitrust.org/cgi/pt?id=mdp.39015008517792>.

³² Doctors are subject to a vast array of drug promotion, which includes detailing (sales calls to doctors’ offices), direct mailings, free drug samples, medical journal advertising, sponsored continuing medical education programs, and media advertising, while pharmacists respond to consumer demand and compete with other pharmacies on price. ALISON MASSON & ROBERT L. STEINER, *GENERIC SUBSTITUTION AND PRESCRIPTION DRUG PRICES: ECONOMIC EFFECTS OF STATE DRUG PRODUCT SELECTION LAWS* 7 (1985); STUART O. SCHWEITZER, *PHARMACEUTICAL ECONOMICS AND POLICY* 87–93 (2d ed. 2007).

not equivalent to the new brand version.³³

E. *Timing*

A central issue in both settlements and product hopping involves timing. Product hopping is most successful when brand firms not only can avoid state DPS laws but also can switch the market before generic entry. Brand firms often stop promoting the old version of the drug, switching their marketing to the new product and offering the “uncontested message” of the new product’s superiority.³⁴ Patients who switch to the new drug are unlikely to switch back.³⁵

The importance of timing was recognized by the Final Report on the pharmaceutical industry issued by the European Commission, which concluded that brands would suffer reduced sales and prices if generics entered the market before or at the same time as the new product.³⁶ Numerous comments revealed brand firms’ emphasis on timing. One company conceded that “[o]nce the patient is switched” to the new product, “the physician does not have to, cannot and will not switch him to a generic,” and “more important: the pharmacist cannot substitute!!”³⁷

F. *Combination of Activities*

The timing of product hopping matters significantly. As discussed above, brand firms have a considerable interest in delaying generic entry until after they can switch the market to the new product. Analyzing conduct in the pharmaceutical industry presents significant difficulty because companies use an array of nuanced activity to forestall entry.³⁸

Firms employ a combination of settlements and product hopping to ensure that they can switch to a new version before generics enter the market on the old version. The value of the conduct in combination is that a settlement that prevents patent challenges for a period of time—even if less than the duration of the patent—allows the brand to switch the market to the new product. So by the time, years later, that the generic enters, the market will have already migrated to the new

³³ Leffler et al., *supra* note 28, at 5.

³⁴ *Id.* at 51.

³⁵ *Id.* at 51–55.

³⁶ EUR. COMM’N, PHARMACEUTICAL SECTOR INQUIRY FINAL REPORT ¶¶ 3, 1010 (2009), available at http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/staff_working_paper_part1.pdf.

³⁷ *Id.* ¶ 1028 (quoting a pharmaceutical company statement).

³⁸ The complication is aggravated by firms’ different business models and market strategies. For example, companies consider actions in the context of a long-term product evolution, and generics take different licensing positions with respect to authorized generics.

product. As a result, the generic, which can no longer take advantage of state DPS laws, fails to provide meaningful competition.

Brand firms' use of citizen petitions filed with the FDA could be a valuable addition to this strategy. By requesting that the FDA make a decision on safety and efficacy—often by reviewing a wealth of material and studies—brands could buy additional time in which they delay generic entry. This delay could make the difference between a brand (1) facing generic competition on the old version of a drug and (2) switching the market to a new version.

How legitimate are the citizen petitions that brands file against generics? How successful are citizen petitions generally? This Article sheds light on these questions by conducting the first empirical study of the conduct.

II. CITIZEN PETITIONS: OVERVIEW

This Part introduces citizen petitions, explaining what they are and what types of parties file them. It then discusses several concerns with them raised by government officials. It concludes by highlighting a 2007 amendment designed to reduce the incidence of citizen petitions.

A. Introduction

The First Amendment ensures that Congress cannot abridge “the right of the people . . . to petition the Government” to take a particular action.³⁹ In 1975, Congress enacted the Administrative Procedure Act (APA), which required government agencies to provide the public with the right to petition for the issuance, amendment, or repeal of a rule.⁴⁰ The FDA allows individuals to express safety, scientific, or legal issues in such a petition regarding a product.⁴¹

Citizen petitions are a means by which any “interested person” can request that the FDA “issue, amend, or revoke a regulation or order,” or “take or refrain from taking any other form of administrative action.”⁴²

³⁹ U.S. CONST. amend. I (“Congress shall make no law . . . abridging the freedom . . . to petition the Government for a redress of grievances.”).

⁴⁰ 5 U.S.C. § 553(e) (2006); see also Stacey B. Lee, *Is a Cure on the Way?*, 20 KAN. J.L. & PUB. POL’Y 98, 108–09 (2010).

⁴¹ 21 C.F.R. § 10.30(a) (2012); *The Generic Drug Maze: Speeding Access to Affordable, Life-Saving Drugs: Hearing Before the S. Spec. Comm. on Aging*, 109th Cong. 6 (2006) [hereinafter *Generic Drug Maze Hearing*], available at <http://aging.senate.gov/publications/7202006.pdf> (statement of Gary Buehler, Director, Office of Generic Drugs, U.S. Food and Drug Administration); see also 21 C.F.R. § 10.30(b)(B) (requiring petitions to state factual and legal grounds for requests).

⁴² 21 C.F.R. §§ 10.25, 10.30.

All citizen petitions must include the “action requested,” particularly the “rule, order, or other administrative action” that the petitioner seeks to “issue, amend or revoke.”⁴³ Petitions also must disclose a “[s]tatement of grounds,” including “the factual and legal grounds for the petition.”⁴⁴

Citizen petitions additionally must describe any environmental effects of the requested action.⁴⁵ And if requested by the Commissioner of Food and Drugs, they must address the petitions’ economic impact, in particular, effects on “(1) cost (and price) increases to industry, government, and consumers; (2) productivity of wage earners, businesses, or government; (3) competition; (4) supplies of important material, products, or services; (5) employment; and (6) energy supply or demand.”⁴⁶

Citizen petitions have been filed by three types of filers. First, brand firms file petitions, often to request denial of a generic’s ANDA. These petitioners raise issues related to safety and efficacy of the generic drug. And they question whether generics are bioequivalent, such that the body can absorb the drug similarly.

Second, generics file petitions to obtain FDA approval in order to submit an ANDA. They also seek to ensure that later-filing ANDAs have sufficient labeling and efficacy or safety profiles. Finally, first-filing generics request that the FDA not approve other ANDAs until the end of 180-day exclusivity.

Third, other parties, such as universities, doctors, and hospitals, file petitions to raise safety concerns or to obtain industry guidelines for studies on particular drugs.

B. *Potential Concerns*

Several leading officials have observed that many citizen petitions are filed on questionable grounds. The Director of the Office of Generic Drugs in the FDA’s Center for Drug Evaluation and Research (CDER) is fully aware of this issue. In 2006, Director Gary Buehler explained in a Senate hearing on citizen petitions that “it is very rare that petitions present new issues that CDER has not fully considered.”⁴⁷ In fact, even if the petition process could be valuable, in theory, or legitimately used,

⁴³ 21 C.F.R. § 10.30(b)(A); *Comment on Regulations: Making Your Voice Heard at FDA: How to Comment on Proposed Regulations and Submit Petitions*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/AboutFDA/ContactFDA/CommentonRegulations/default.htm> (last updated Feb. 7, 2008).

⁴⁴ 21 C.F.R. § 10.30(b)(B).

⁴⁵ *Id.* § 10.30(b)(C).

⁴⁶ *Id.* § 10.30(b)(D).

⁴⁷ *Generic Drug Maze Hearing*, *supra* note 41, at 15 (statement of Gary Buehler, Director, Office of Generic Drugs, U.S. Food and Drug Administration).

“very few of these petitions on generic drug matters have presented data or analyses that significantly altered FDA’s policies.”⁴⁸ Despite this, “the agency must nevertheless assure itself of the fact by carefully reviewing these citizen petitions.”⁴⁹

Similarly, FDA Chief Counsel Sheldon Bradshaw commented that citizen petitions “appear designed not to raise timely concerns with respect to the legality or scientific soundness of approving a drug application, but rather to delay approval by compelling the agency” to examine arguments that could have been made previously.⁵⁰

Director Buehler noted that, of the 42 FDA responses to citizen petitions filed between 2001 and 2005, the agency denied 33, denied 3 in part, and granted 6.⁵¹ Even these figures overstated the petitions’ contributions. The reason is that even petitions that are granted often do not change the outcome. Buehler explained that “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.”⁵²

Many of the petitions, for example, request that the ANDA applicant submit additional bioequivalence studies. But ANDA applicants already submit such studies as part of the application process itself. In addition, petitions often request studies under “fed and fasting” conditions, in other words, taking the medication with and without food. But again, for many of the drugs, the FDA already requires this in industry guidelines outlining what is generally suggested to achieve FDA approval.⁵³

To give one example, the FDA granted in part and denied in part Ortho-McNeil’s petition concerning ANDAs referencing its brand drug, Ditropan XL.⁵⁴ The petition requested that “all bioequivalence studies be conducted under both fed and fasting conditions.”⁵⁵ The FDA “granted in part” the request “[b]ecause we expect generic . . . applicants

⁴⁸ *Id.*

⁴⁹ *Id.*

⁵⁰ Marc Kaufman, *Petitions to FDA Sometimes Delay Generic Drugs*, WASH. POST., July 3, 2006, at A1 (quoting Sheldon Bradshaw, Chief Counsel, U.S. Food & Drug Admin.).

⁵¹ *Generic Drug Maze Hearing*, *supra* note 41, at 15 (statement of Gary Buehler, Director, Office of Generic Drugs, U.S. Food and Drug Administration).

⁵² *Id.* For a fuller discussion of this issue, see *infra* notes 85–100 and accompanying text.

⁵³ See generally CTR. FOR DRUG EVALUATION AND RESEARCH, U.S. DEPT. OF HEALTH AND HUMAN SERVS., GUIDANCE FOR INDUSTRY: FOOD-EFFECT BIOAVAILABILITY AND FED BIOEQUIVALENCE STUDIES (2002), available at http://www.fda.gov/downloads/regulatory_information/guidances/ucm126833.pdf.

⁵⁴ FDA Response to Ortho-McNeil Pharmaceuticals, Inc. Citizen Petition, Docket No. FDA-2005-P-0002, at 1 (Nov. 9, 2006) [hereinafter FDA Response to Ortho-McNeil], available at <http://www.regulations.gov/#!documentDetail;D=FDA-2005-P-0002-0002>.

⁵⁵ *Id.*

to measure [the active ingredients] in both fasting and fed studies.”⁵⁶ But this “grant in part” did not seem to have any effect since, under the FDA’s “Food Effect Guidance,” all drugs of this type necessarily must demonstrate bioequivalence under fed and fasting conditions.⁵⁷ The petition nonetheless delayed generic entry, with the FDA taking more than 14 months to file a substantive response.⁵⁸

Even if citizen petitions offer little incremental value, the FDA is forced to spend considerable time responding to the petitions. For starters, the agency is required to address the merits of every citizen petition submitted.⁵⁹ This has led to a backlog at the FDA. Many petitions contain “detailed analysis and precise scientific documentation” and require review by “multiple disciplines within CDER.”⁶⁰ Additionally, the CDER conducts a “thorough legal review” since petitioners often “submit non-scientific petitions that raise purely legal questions related to ANDA approvals.”⁶¹

Part of the reason for the backlog can be traced to the FDA’s response to petitions. Before 2007, the agency endeavored to respond to petitions within 180 days, but this response could come in any form, including approval or denial of the petition (each in whole or in part) or a tentative response indicating that the agency had not yet been able to reach a decision.⁶² In other words, it often took the FDA longer than the six-month time frame to reach a final decision. Consider Aventis, which filed a petition in 2003 concerning Lovenox, a drug used to prevent blood clots. The FDA did not reach a final decision until 2010, a total of 2,644 days after the petition was first filed.⁶³

Congress held hearings in 2006 on citizen petitions and delays in the process. Testifying from the government were Gary Buehler and Jon Leibowitz, then Commissioner (and subsequent Chairman) of the

⁵⁶ *Id.* at 6.

⁵⁷ *Id.* For further discussion of this issue, see *infra* notes 85–100 and accompanying text.

⁵⁸ *Id.* at 1.

⁵⁹ *Generic Drug Maze Hearing*, *supra* note 41, at 14 (statement of Gary Buehler, Director, Office of Generic Drugs, U.S. Food and Drug Administration); see also 21 C.F.R. § 10.30(e) (2012) (“The Commissioner shall . . . rule upon each petition filed . . . [and] shall furnish a response to each petitioner within 180 days of receipt of the petition.”).

⁶⁰ *Generic Drug Maze Hearing*, *supra* note 41, at 14 (statement of Gary Buehler, Director, Office of Generic Drugs, U.S. Food and Drug Administration).

⁶¹ *Id.*

⁶² 21 C.F.R. § 10.30(e)(2) (noting that “the Commissioner shall furnish a response to each petitioner within 180 days of receipt of the petition” and that the response will “(i) [a]pprove the petition . . . ; (ii) [d]eny the petition; or (iii) [p]rovide a tentative response, indicating why the agency has been unable to reach a decision on the petition”).

⁶³ Although the FDA stated in the response that the petition was granted in part and denied in part, the petition was effectively denied because the FDA concluded that Aventis’s requests for additional bioequivalence studies were unnecessary. FDA Response to Aventis Pharmaceuticals, Inc. Citizen Petition, Docket No. FDA-2003-P-0273, at 1, 45 (July 23, 2010), available at <http://www.regulations.gov/#!documentDetail;D=FDA-2003-P-0273-0041>.

Federal Trade Commission.⁶⁴ From private industry were Heather Bresch, senior vice president at Mylan Laboratories, and Mark Merritt, president and CEO of Pharmaceutical Care Management Association.⁶⁵ Each highlighted some of the concerns presented by citizen petitions.

C. 2007 Amendment

As a result of the 2006 hearing,⁶⁶ Congress enacted Section 914 of Title IX of the Food and Drug Administration Amendments Act (FDAAA) of 2007,⁶⁷ which added a new rule, known as section 505(q), to citizen petitions.⁶⁸ The legislature sought to ensure that the FDA did not delay approval of drug applications unless a petition was “necessary to protect the public health.”⁶⁹ As Senator Edward Kennedy explained: “The citizen petition provision is designed to address attempts to derail generic drug approvals. Those attempts, when successful, hurt consumers and the public health.”⁷⁰

Section 505(q) applies to “certain petitions that request that FDA take any form of action related to a pending ANDA.”⁷¹ It also requires petitioners to ensure that they have not delayed filing the petition.⁷² Congress sought to ensure that companies do not file “eleventh hour petitions” or petitions on the eve of drug approval for the purpose of delay. Any petition that reasonably could delay the approval of a pending NDA or ANDA application falls under section 505(q).

Section 505(q) adds certification and verification components to citizen petitions covered by the legislation. Petitioners must certify that their allegations are true to the best of their knowledge and that they are

⁶⁴ *Generic Drug Maze Hearing*, *supra* note 41, at III.

⁶⁵ *Id.*

⁶⁶ See 153 CONG. REC. 10,962–63 (2007) (statement of Sen. Herb Kohl).

⁶⁷ 21 U.S.C. § 355(q) (2006).

⁶⁸ CTR. FOR DRUG EVALUATION AND RESEARCH, U.S. DEPT. OF HEALTH AND HUMAN SERVS., GUIDANCE FOR INDUSTRY: CITIZEN PETITIONS AND PETITIONS FOR STAY OF ACTION SUBJECT TO SECTION 505(Q) OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT 1 (2011) [hereinafter GUIDANCE FOR INDUSTRY], available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM079353.pdf>.

⁶⁹ Federal Food, Drug, and Cosmetic Act (FFDCA) § 505(q)(1)(A), 21 U.S.C. § 355(q)(1)(A) (2006). Because the new legislation was designed to prevent delay, two categories of petitions that do not pose this concern are exempt. First, the section does not apply to petitions filed by ANDAs relating to their applications. GUIDANCE FOR INDUSTRY, *supra* note 68, at 7. Second, it does not cover petitions that “relate solely to the timing of approval” of a Paragraph IV application. *Id.*

⁷⁰ 153 CONG. REC. 25,047 (2007).

⁷¹ GUIDANCE FOR INDUSTRY, *supra* note 68, at 2. It also applies to Section 505(b)(2) applications, which are viewed as “hybrids,” containing more data than ANDAs but less than NDAs. REGULATORY PROFESSIONALS, INC., THE 505(B)(2) NEW DRUG APPLICATION—A RAPID APPROVAL ROUTE 1 (2008), [http://www.regprofessional.com/resources/505\(b\)\(2\).pdf](http://www.regprofessional.com/resources/505(b)(2).pdf).

⁷² See 153 CONG. REC. 25,047 (2007).

not withholding unfavorable information.⁷³ Because the Act does not provide an opportunity for petitioners to cure the certification and verification requirements, it applies only to petitions filed after September 27, 2007, the date of enactment.⁷⁴

Section 505(q) requires that the FDA act quickly in addressing petitions. Under section 505(q)(1)(F), the agency must take final action no later than 180 days after the petition's filing date.⁷⁵ This period cannot be extended for any reason, even if the FDA finds that a delay in a related pending application is required.⁷⁶ In other words, even if the agency concludes that the petition raises legitimate issues warranting delay in approving a pending ANDA, the FDA must still respond to the petition within the 180-day timeframe.

In addition, section 505(q) allows the Secretary of Health and Human Services to deny a petition if she "determines that a petition or a supplement to the petition was submitted with the primary purpose of delaying the approval of an application and the petition does not on its face raise valid scientific or regulatory issues."⁷⁷

The FDA released a Draft Guidance for Industry in 2009 to explain its interpretation of section 505(q).⁷⁸ The agency made clear that "delay" would be interpreted expansively to apply to "any reasonable theory" of delay.⁷⁹

III. STUDY

This Part summarizes the results of an empirical study of all citizen petitions filed between 2001 and 2010. It begins by explaining our general methodology. The second section discusses our parsing of "mixed" FDA decisions to determine essential grants and denials. Section C then presents our results, covering (1) the number of petitions filed, (2) the target of brand petitions, (3) the categories of brand petitions, (4) the overall win rate, (5) the brand win rate, and (6) the

⁷³ FFDCA § 505(q)(1)(H).

⁷⁴ *Id.*

⁷⁵ *Id.* § 505(q)(1)(F).

⁷⁶ *Id.* Any action taken by the FDA at the end of this 180-day period, or any expiration of the period, is considered final, subject to immediate review by the courts. *Id.* § 505(q)(2)(A); GUIDANCE FOR INDUSTRY, *supra* note 68, at 11. In addition, section 505(q) provides that courts are to dismiss civil actions filed against the Secretary of the Department of Health and Human Services with respect to any issues raised in a petition before the FDA's final approval. FFDCA § 505(q)(2)(B).

⁷⁷ FFDCA § 505(q)(1)(E).

⁷⁸ CTR. FOR DRUG EVALUATION AND RESEARCH, U.S. DEPT. OF HEALTH AND HUMAN SERVS., DRAFT GUIDANCE: CITIZEN PETITIONS AND PETITIONS FOR STAY OF ACTION SUBJECT TO SECTION 505(Q) OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT (Jan. 2009), *available at* <http://www.regulations.gov/#!documentDetail;D=FDA-2009-D-0008-0002>. In 2011, the FDA released a final version of this guidance. *See* GUIDANCE FOR INDUSTRY, *supra* note 68.

⁷⁹ GUIDANCE FOR INDUSTRY, *supra* note 68, at 7.

brand win rate against generics.

A. *Methodology: General*

We located citizen petitions through www.regulations.gov, an online database that includes the regulations, petitions, and comments for more than 300 federal agencies, including the FDA. We ran searches in this database to locate all citizen petitions filed with the FDA.⁸⁰

The study covers all petitions related to current or pending drugs filed between 2001 and 2010. It excludes animal drugs as well as “ANDA suitability petitions” in which a generic company asks the FDA to confirm that a drug is suitable for an ANDA submission.⁸¹

In the www.regulations.gov database, citizen petitions take the form “FDA-year-P-four-digit number.”⁸² For example, a citizen petition filed by Biovail in 2005 concerning Wellbutrin XL had the docket number FDA-2005-P-0498. We focused on “P” petitions since they were the only ones to target pharmaceutical drugs.

In the database, we ran searches that took the form “FDA-year-P.” For example, to run a search for all petitions filed with the FDA in 2005, we used the search term “FDA-2005-P” in the “Keyword or ID” box. This search yielded 1477 results. To make these results more manageable, we viewed them by docket folder, which collected in one location all the materials in a single case.

The docket folder includes citizen petitions as well as accompanying supplements, comments, and FDA responses. We examined each folder to find all petitions filed with the FDA regarding current or pending drugs. We then examined the citizen petition itself, as well as the FDA’s substantive response. We did not examine supplements to petitions, documents containing scientific studies, or third-party comments on the petitions.

For petitions filed after 2007 (when the database became available), we double-checked our results with the “Citizen Petition Tracker” (Tracker), a frequently-updated, easily-searchable table available on www.fdalawblog.net that lists citizen petitions, accompanied by links to

⁸⁰ The FDA website provides a chronological list of petitions and advisory opinions filed with the agency from 2000 to January 2008. At the time this Article went to press, the agency, after implementing a new docketing system in 2008, had not yet completed updating and uploading these files. For that reason, we utilized the www.regulations.gov site rather than the incomplete FDA site. It is possible that a few petitions listed on the FDA website have not yet appeared on www.regulations.gov, though this should not materially affect the results.

⁸¹ Suitability petitions ask the FDA to conclude that a drug was removed from the market for reasons other than safety or efficacy. In these cases, such as those involving drug labeling issues, the agency could conclude that the drug is suitable for an ANDA.

⁸² “P” denotes petition.

the petitions and accompanying FDA responses.⁸³ The Tracker confirmed the results we obtained on regulations.gov. Every response listed in the Tracker was included in our results, and we did not locate any petitions that were not covered in the Tracker.

B. *Methodology: Mixed Decisions*

One of the difficulties involved in reviewing FDA rulings on citizen petitions concerns the number of petitions that are not clear grants or denials. The FDA sometimes issues “mixed” decisions, which grant in part and deny in part the petition. Although these determinations technically are mixed, one of the findings is often a formality that has no practical significance. This section provides examples of decisions that, upon close analysis, are not truly mixed. This study parsed every mixed decision to reach a conclusion on the petition’s effective outcome.⁸⁴

The FDA sometimes “grants” requests that reflect standard industry practices that the agency would require as a matter of course. In addition to the examples discussed below concerning Biovail’s depression drug Wellbutrin XL⁸⁵ and Sanofi’s insomnia drug Ambien,⁸⁶ several other examples demonstrate this phenomenon.

In the first, Purdue Pharma and Endo Pharmaceuticals each filed petitions relating to certain drug products containing opioids (pain suppressants), requesting that the FDA not approve any application without conducting additional studies or requiring the use of warnings.⁸⁷ The FDA explained that most of the petitioners’ requests were consistent with its standard practice. The agency already had been “requiring all NDA and ANDA applicants for modified-release opioid drug products to submit appropriate data from in vitro alcohol dissolution tests.”⁸⁸ As a result, the agency “granted in part” the petitions “to the extent that they request actions that we have already taken or are taking.” At the same time, it denied “the remaining requests.”⁸⁹

Another example of mixed results that are essentially denials occurs when the FDA denies a request to require certain bioequivalence or efficacy studies in all instances, but grants the requirement if the

⁸³ *FDC Act § 505(q) Citizen Petition Tracker*, FDA LAW BLOG, http://www.fdalawblog.net/fda_law_blog_hyman_phelps/files/505q_cps_chart_cmb.xls (last visited Aug. 23, 2012).

⁸⁴ The two authors independently made these determinations. They agreed on the outcome in 47 of 51 petitions. They resolved the disputed 4 by consensus.

⁸⁵ See *infra* Part V.A.

⁸⁶ See *infra* Part V.B.

⁸⁷ FDA Response to Purdue Pharmaceuticals Citizen Petition, Docket No. FDA-2007-P-0003, at 1–2 (Apr. 30, 2008), available at <http://www.regulations.gov/#!documentDetail;D=FDA-2007-P-0003-0009>.

⁸⁸ *Id.* at 4.

⁸⁹ *Id.* at 12.

ANDA applicant's studies later turn out to be insufficient.

For example, Sanofi-Aventis filed a petition relating to the drug Eloxatin, which is used with other drugs to prevent the spread of colon cancer.⁹⁰ Sanofi requested that the FDA not approve ANDA applicants that did not require certain testing. The agency denied this request to the extent that the petition presented a "theoretical concern," and granted the petition in that the agency intended to "closely examine" the issues Sanofi raised to ensure the ANDA complied in the future with the FDA's guidance documents.⁹¹ The partial grant was not central since it related to future studies to be conducted only if later deemed necessary.

A final example occurs when the FDA grants a request to consider issues for later ANDA filers while denying a request to strip a company of its ANDA or NDA status on the basis that the drug was not deemed safe or effective.

This scenario occurred in EKR Therapeutics' petition relating to the blood-pressure drug Cardine I.V. EKR's petition asked the FDA to strip Teva of its NDA for the product, to refuse to allow Teva to relaunch (while not giving a chance to cure deficiencies), and to request all future NDA and ANDA applicants to "adequately characterize any differences in inactive ingredients" and provide the results of certain bioequivalence studies.⁹²

The FDA concluded that there were no deficiencies in Teva's NDA and thus denied the petitioner's request to strip Teva's NDA status.⁹³ But the agency "granted" the request for future applicants that may need to conduct the requested bioequivalence study. The FDA thus essentially denied the petition in relation to Teva while granting it for future applicants.⁹⁴

In addition to essential denials, the FDA sometimes issues mixed decisions that are essential grants. This often occurs when a request affects the FDA's approval process for NDAs or ANDAs. For example, Salix Pharmaceuticals filed several petitions relating to the drug Colazal, which treats ulcerative colitis.⁹⁵ The petitions asked the FDA to decline to approve ANDAs without additional tests and to draft industry

⁹⁰ FDA Response to Sanofi-Aventis Citizen Petition, Docket No. FDA-2006-P-0025, at 2 (May 22, 2009), *available at* <http://www.regulations.gov/#!documentDetail;D=FDA-2006-P-0025-0017>.

⁹¹ *Id.* at 9.

⁹² FDA Response to EKR Therapeutics Citizen Petition, Docket No. FDA-2008-P-0621, at 1 (May 29, 2009), *available at* <http://www.regulations.gov/#!documentDetail;D=FDA-2008-P-0621-0006>.

⁹³ *Id.* at 12.

⁹⁴ *Id.*

⁹⁵ FDA response to Salix Pharmaceuticals Citizen Petition, Docket No. FDA-2005-P-0314, at 2 (Dec. 28, 2007), *available at* <http://www.regulations.gov/#!documentDetail;D=FDA-2005-P-0314-0004>.

guidance on bioequivalence standards.⁹⁶

The FDA granted in part and denied in part the petition.⁹⁷ The agency denied many of Salix's requested studies on the grounds that (1) they were not necessary for an ANDA applicant to prove bioequivalence, (2) the current standards applied by the FDA were sufficient, and (3) industry guidance would not be helpful due to the varying nature of the drug.⁹⁸

At the same time, the FDA granted in part the request since, because of a change in Colazal's labeling, some of the tests Salix requested (such as an additional fed and fasting study) were needed to prove bioequivalence.⁹⁹ The grant affected the FDA's approval process for the drug because it added requirements for ANDA applicants, including Roxane Laboratories, whose ANDA was the first generic version of Colazal approved.¹⁰⁰

These are but a handful of the many cases in which the FDA formally reached a mixed result of grant in part and denial in part. Table 1A in the Appendix presents the results of our careful analysis of the mixed determinations. We conclude that 12 out of 51 (24%) were essentially granted; 23 (45%) were essentially denied; and 16 (31%) truly were mixed.

C. Results

1. Total Petitions

Table 1 depicts the total number of citizen petitions filed from 2001 through 2010. This table includes every citizen petition we could locate, including those with incomplete information (such as no FDA response). Table 1 shows that between 10 and 37 petitions were filed each year, with a mean of 26 and a median of 31 petitions. The number increased in 2004, most likely because, in that year, several drug companies filed separate petitions regarding the same group of drugs.¹⁰¹

⁹⁶ *Id.* at 1–2.

⁹⁷ *Id.* at 1.

⁹⁸ *Id.* at 6, 11, 22, 25. The “variety of release mechanisms” of the drug signified that “a single bioequivalence recommendation” was not appropriate. *Id.* at 6.

⁹⁹ *Id.* at 21, 26.

¹⁰⁰ *Drugs@FDA*, U.S. FOOD & DRUG ADMIN., <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.DrugDetails> (last visited Aug. 23, 2012).

¹⁰¹ The petitions filed concerning the pain-relieving skin patch, Duragesic, provide one such example. FDA Consolidated Response to ALZA Citizen Petition, Docket No. FDA-2004-P-0465, <http://www.regulations.gov/#!docketDetail;dc=FR%252BPR%252BN%252BO%252BSR;rpp=25;po=0;D=FDA-2004-P-0465>. Each of the petitions raised modestly different points, including the suggestion of requirements of additional skin testing, risk management plans, and additional aspects of bioequivalence. *Id.* The FDA denied these requests in a consolidated response, concluding that the drug was safe and additional studies were unnecessary. *Id.*

The data from Table 1 show that the number of citizen petitions has increased over time. The filings increased in 2004, and after a drop in 2005, stayed at or above 30 in each year from 2006 through 2010. Nor was there a decrease in the number of petitions filed after 2007, the year the law changed to limit FDA review to 180 days. In the three years before the passage of the 2007 amendment, there were an average of 27 filings a year. In the three years after enactment, the average climbed to 34 filings a year.

Finally, Table 1 shows that (rounded to the nearest percent, as with all the figures discussed in this Article) 68% of petitions were filed by brand companies, 22% by generics, and the remaining 10% by other parties.¹⁰²

As required by the 2007 amendment,¹⁰³ the FDA has reported to Congress the number of 505(q) petitions, including those delayed.¹⁰⁴ This universe, however, is smaller than ours because our study reaches beyond pending ANDAs to cover ANDAs that have not yet been filed as well as those that have already been approved. These additional categories threaten similarly concerning anticompetitive effects since they also could be used to delay generic entry.

Table 1
Total Filings Categorized by Identity of Petitioner

	Total	Brand Filer	Generic Filer	Other/ Uncategorized
2001	10	4	4	2

¹⁰² The “other” category includes research institutions, universities, hospitals, doctors, public policy groups, and other concerned individuals. Also included are uncategorized filers, in particular, law firms filing petitions on behalf of entities that could not be ascertained.

¹⁰³ 21 U.S.C. § 355(q)(3) (2006).

¹⁰⁴ The FDA reported 2 ANDA applications delayed out of 21 section 505(q) petitions filed from 2007 to 2008, U.S. FOOD & DRUG ADMIN., ANNUAL REPORT ON DELAYS IN APPROVALS OF APPLICATIONS RELATED TO CITIZEN PETITIONS AND PETITIONS FOR STAY OF AGENCY ACTION FOR FISCAL YEAR 2008, at 3 (2009), *available at* <http://www.hpm.com/pdf/FDA%20FY2008%20505q%20CP%20Report.PDF>; 1 ANDA application delayed out of 31 section 505(q) petitions filed between 2008 and 2009, U.S. FOOD & DRUG ADMIN., SECOND ANNUAL REPORT ON DELAYS IN APPROVALS OF APPLICATIONS RELATED TO CITIZEN PETITIONS AND PETITIONS FOR STAY OF AGENCY ACTION FOR FISCAL YEAR 2009, at 3 (2010) [hereinafter 2009 FDA REPORT], *available at* <http://www.hpm.com/pdf/FDA%20FY2009%20505q%20CP%20Report.PDF>; and 1 ANDA application delayed out of 20 section 505(q) petitions filed between 2009 and 2010, U.S. FOOD & DRUG ADMIN., THIRD ANNUAL REPORT ON DELAYS IN APPROVALS OF APPLICATIONS RELATED TO CITIZEN PETITIONS AND PETITIONS FOR STAY OF AGENCY ACTION FOR FISCAL YEAR 2010, at 3 (2011) [hereinafter 2010 FDA REPORT], *available at* <http://www.hpm.com/pdf/blog/FDA%20FY2010%20505q%20CP%20Report.PDF>.

2002	17	6	10	1
2003	16	15	1	0
2004	32	23	2	7
2005	19	15	2	2
2006	32	24	3	5
2007	30	21	6	3
2008	32	23	9	0
2009	37	26	9	2
2010	33	19	10	4
Total	258	176	56	26
Percentage	100%	68%	22%	10%

2. Targets of Brand Petitions

Concerns of delay have typically been raised in the context of citizen petitions filed by brand firms. For that reason, we examined brand petitions' targets, in other words, the companies whose drugs were the subject of petitions. Like Table 1, Table 2 covers every petition filed between 2001 and 2010. It shows that, for the past 10 years, 78% of brand filings were against generics. In every year except 2003, generics were the target of at least 67% of petitions filed by brand firms.

Table 2
Targets of Brand Petitions¹⁰⁵

	Brand v. Brand	Brand v. Generic	Brand v. Other ¹⁰⁶
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¹⁰⁵ Some percentages in Table 2 (and the other Tables in this Article) do not equal 100 due to rounding.

¹⁰⁶ The "other" category here represents those petitions for which the target of the petition was unascertainable.

2001	0	0%	3	75%	1	25%
2002	1	17%	4	67%	1	17%
2003	7	47%	7	47%	1	7%
2004	0	0%	19	83%	4	17%
2005	0	0%	12	80%	3	20%
2006	2	8%	17	71%	5	21%
2007	2	10%	16	76%	3	14%
2008	0	0%	21	91%	2	9%
2009	0	0%	21	81%	5	19%
2010	0	0%	18	95%	1	5%
Total	12	7%	138	78%	26	15%

What are the grounds on which brands are filing petitions? The four main categories are safety concerns, bioequivalence requests, additional studies, and label concerns (such as requests for specific language and warnings). Other reasons include misbranding of drugs, changes in the Orange Book,¹⁰⁷ enforcement of a company's exclusivity periods, and patent infringement issues.

Table 2A in the Appendix shows that among brand petitions, 28% request bioequivalence studies, 20% request additional studies, 13% challenge a drug's safety, 7% address desired label changes, and 31% respond to other concerns.¹⁰⁸

3. Citizen Petition Success Rates

Figure 1 and Table 3 show the success rate for citizen petitions by year from 2001 to 2010. Unlike Tables 1 and 2, which cover all petitions, Figure 1 and Table 3 cover only petitions on which the FDA substantively ruled. In particular, they include only those petitions

¹⁰⁷ The Orange Book is an FDA publication that contains patents that brand firms believe would be infringed by generics. *Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/cder/ob/> (last updated Jun. 13, 2012).

¹⁰⁸ Petitions that fell into multiple categories were counted once in each of the categories.

granted or denied by the agency.

Figure 1 and Table 3 do not include petitions that were withdrawn or pending, or for which there was insufficient information regarding the FDA response (most typically, where the response does not appear on the regulations.gov website).¹⁰⁹

¹⁰⁹ There is no evidence that including petitions currently pending would have materially changed our results given how few petitions were pending at the time of the study and the similarity of the issues in these petitions.

Figure 1
Success Rate of Citizen Petitions

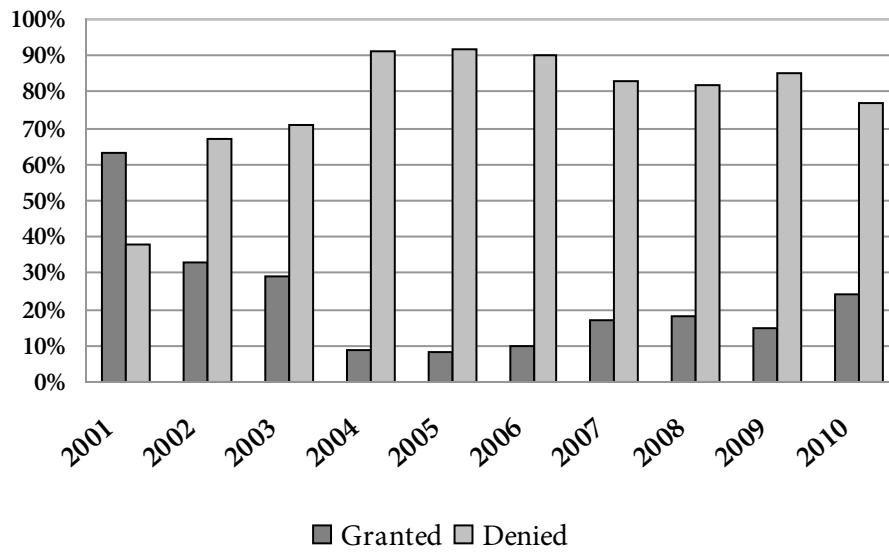


Table 3 presents these results in table form.

Table 3
Success Rate of Citizen Petitions

	Granted		Denied		Total
2001	5	63%	3	38%	8
2002	3	33%	6	67%	9
2003	4	29%	10	71%	14
2004	2	9%	21	91%	23
2005	1	8%	12	92%	13
2006	1	10%	9	90%	10
2007	3	17%	15	83%	18
2008	4	18%	18	82%	22
2009	4	15%	23	85%	27
2010	4	24%	13	77%	17
Total	31	19%	130	81%	161 ¹¹⁰

Table 3 and Figure 1 reveal that the FDA granted 19% of petitions and denied 81%. The grant rate was highest in 2001 (63%) and 2002 (33%). In the next eight years, it fluctuated between 8% and 29%, with a mean of 16% and median of 18%. The mean and median denial rates from 2003 through 2010 were both 84%.

Table 3 and Figure 1 show that the grant rate for all petitions increased after the 2007 amendment. In the three years before the amendment, the FDA granted 12% and denied 88% of petitions. In the three years after the amendment, the agency granted 18% and denied 82%.¹¹¹

To highlight the relationship between grants and denials, and given the small number of truly mixed decisions, Figure 1 focuses only on the FDA's grants and denials of citizen petitions. The data in Figure 1

¹¹⁰ There are 16 mixed decisions that were not included in Table 3. In addition, we were not able to locate FDA responses for 81 petitions. Together, these 97 petitions explain the difference between the 161 petitions in Table 3 and 258 petitions in Table 1.

¹¹¹ See *supra* Table 3 (comparing average of grants and denials from 2008 to 2010 to average of grants and denials from 2005 to 2007).

involve a close parsing of the mixed decisions to determine those that were essentially granted and those essentially denied. Readers interested in viewing the original data, which does not parse the mixed decisions but which includes the actual number of grants and denials, can find this information in the Appendix, in Figure 1A and Table 3A.¹¹²

The conclusions in the Appendix are similar. Figure 1A provides the “Original Success Rate,” in other words, calculations of petition success rates that do not parse the mixed decisions. In this data set, the FDA granted 15% and denied 85% of cases in which it granted or denied a petition. The grant rate was highest in 2001 (67%), 2002 (29%), and 2003 (31%). In the next seven years, it fluctuated between 0% and 16%, with a mean of 8% and median of 8%. During these seven years, the mean and median denial rates, respectively, were 92% and 92%.¹¹³

4. Brand Win Rate

The success rate discussed in the previous section applies to all petitions. Figure 2 focuses on petitions filed by brand companies. The data accompanying Figure 2 reveal that the FDA granted 22 petitions filed by brands, roughly 19%. And the agency denied 96 petitions, roughly 81%.¹¹⁴

Generics file fewer petitions. But their success rate is higher. As the data reveal, the FDA granted 8 (28%) petitions and denied 21 (72%) of petitions filed by generics.¹¹⁵ In other words, generics enjoyed almost double the success rate of brands when filing petitions.¹¹⁶

The number of brand petitions filed after the 2007 amendment did not decrease. To the contrary, in the three years before the amendment

¹¹² There were a total of 16 truly mixed decisions, that is, petitions not effectively granted or effectively denied. This category consisted of 12 brand petitions (1 each in 2001 and 2007; 3 each in 2006 and 2009; and 4 in 2010) and 4 generic petitions (3 in 2002, and 1 in 2010).

¹¹³ The denial rate of 81% in the text is modestly lower than the 85% figure appearing in Table 3A because denials made up only 66% of the mixed decisions that were effectively grants or denials, less than the 85% of clear denials. *See infra* Appendix.

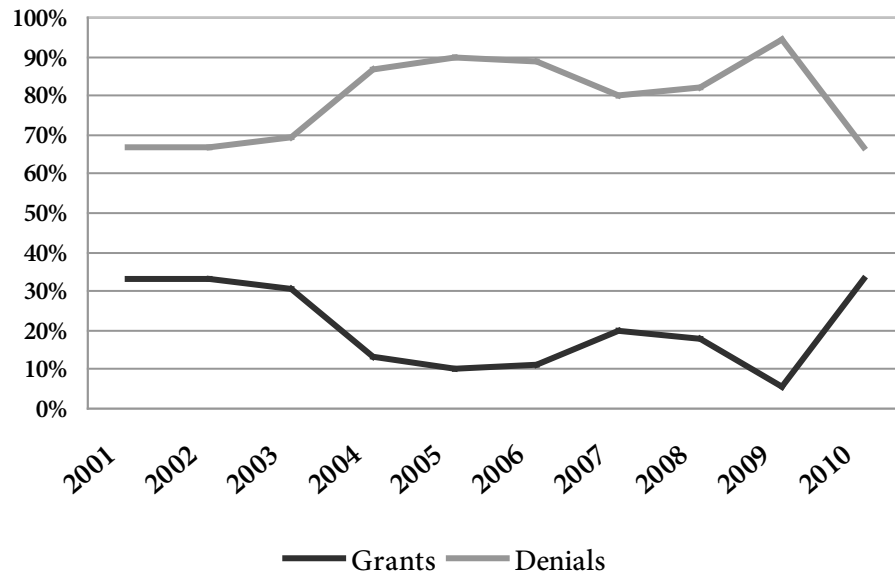
¹¹⁴ For the years between 2001 and 2010, the FDA granted brand petitions 1, 2, 4, 2, 1, 1, 3, 3, 1, and 4 times, in each year, respectively, for a total of 22. The agency denied petitions 2, 4, 9, 13, 9, 8, 12, 14, 17, and 8 times, in each year, respectively, for a total of 96. The total numbers in this section are lower than those in Tables 1 and 2 because of the requirement here of petitions followed by a substantive FDA response.

¹¹⁵ The FDA granted generic petitions 3 times in 2001 and 2009, and 1 time in 2002 and 2008 for a total of 8. The agency denied generic petitions 4 times in 2008 and 2009; 3 times in 2007, and 2010; 2 times in 2002, 2004, and 2005; and 1 time in 2003 for a total of 21. Parties that did not clearly fit the definition of brands or generics filed 26 petitions, all of which were denied.

¹¹⁶ This difference could be explained by the difference in grounds raised in the two sets of petitions. Brands tend to focus on the safety, efficacy, and bioequivalence of ANDA generics, while generics more narrowly ensure that later-filed ANDAs have the same labeling, as well as safety and efficacy profiles.

went into effect, there were 38 brand filings.¹¹⁷ In the three years after, there were 55, an increase of 45%.¹¹⁸

Figure 2
Brand Win Rate



5. Brand Win Rate Against Generics

Brands file petitions against not only generics but also other brand firms. Figure 3 parses the results of Figure 2 to provide the brand success rate against generics. As the data accompanying Figure 3 reveal, the FDA granted 18 petitions filed by brands against generics, roughly 20%. During this period, the agency denied 74 petitions, roughly 80%.¹¹⁹

Although the focus has generally been on brand petitions against

¹¹⁷ In 2005, 2006, and 2007, there were 1, 1, and 3 grants; 9, 8, and 12 denials; and 0, 3, and 1 mixed decisions, respectively, for a total of 38 petitions.

¹¹⁸ In 2008, 2009, and 2010, there were 3, 1, and 4 grants; 14, 17, and 8 denials; and 0, 3, and 5 mixed decisions, respectively, for a total of 55 petitions.

Figure 2 reveals an increase in the brand win rate in 2010. This stems from three decisions that were “granted in part” and “denied in part.” Each of the petitions requested that the FDA require additional studies for ANDA filers. In each of the three petitions, the FDA concluded that at least one of the studies requested was necessary, but the rest were not.

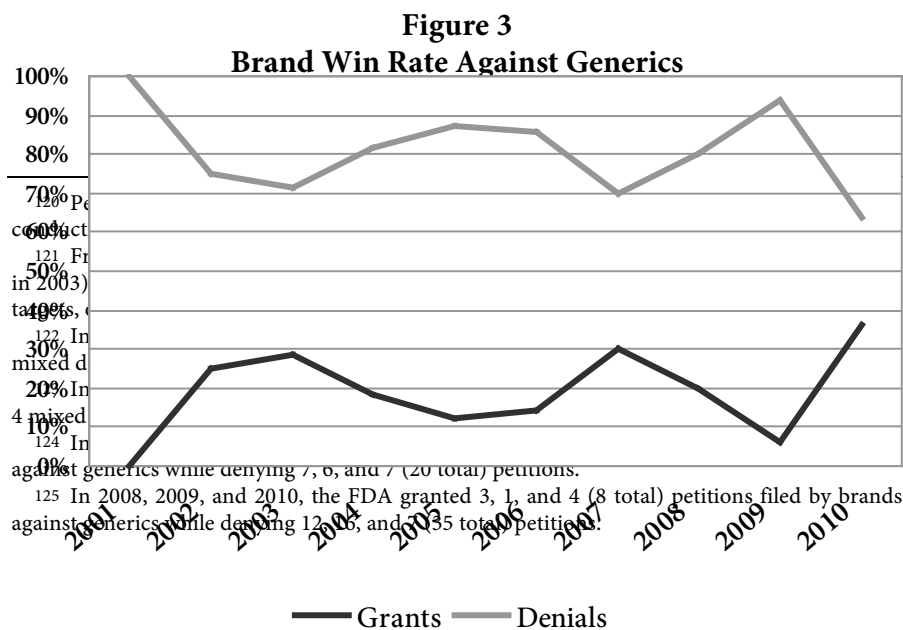
¹¹⁹ From 2001 through 2010, the number of grants each year for brand petitions against generics was 0, 1, 2, 2, 1, 1, 3, 3, 1, and 4, respectively, for a total of 18. The number of denials for brand petitions against generics was 2, 3, 5, 9, 7, 6, 7, 12, 16, and 7, respectively, for a total of 74. Eight of the petitions were “mixed.” Again, the total numbers in this section are lower than those in Tables 1 and 2 because of the focus here on petitions followed by a substantive FDA response.

generics, brands also file petitions to prevent other brands from receiving NDA approvals. These petitions typically request additional safety studies or the enforcement of exclusivity periods (most commonly, pediatric exclusivity¹²⁰).

Brands file fewer petitions against other brands than against generics. But their success rate is higher. As the data show, the FDA granted 3 (37%) petitions against other brands and denied 5 (63%).¹²¹

The number of brand petitions against generics after the 2007 amendment increased significantly. In the three years before the amendment went into effect, there were 28 brand filings against generics.¹²² In the three years after, there were 47. In other words, the number of brand petitions against generics increased from roughly 9 to 16 each year.¹²³

In addition, brands' success rate against generics declined marginally after the enactment of the 2007 amendment. In the three years before the amendment, the FDA granted 20% and denied 80% of brand petitions against generics.¹²⁴ In the following three years, the FDA granted 19% and denied 81% of brand petitions against generics.¹²⁵



IV. CITIZEN PETITIONS: DISCUSSION AND CONCERNS

Part III showed that the overwhelming majority of citizen petitions are denied. The FDA denied 81% of all petitions, including 80% filed by brands against generics. If that is the case, one obvious question is why so many petitions are filed. Do brand firms wish to raise legitimate concerns about generic drugs' safety and efficacy? Or are the petitions filed for reasons having little to do with the merits of the petitions?

This Part hypothesizes that many petitions are filed to delay generic entry. Brand firms have significant incentives and ability to file petitions for this purpose, and the activity fits comfortably in the toolbox of activity delaying generic competition. The Part concludes by showing that the 2007 amendment has not reduced the number of petitions.

A. *Incentives to File Questionable Petitions and Role in Toolkit*

This Article began by discussing settlements and product hopping. Citizen petitions can be used in conjunction with these activities. As stated above, brand drug companies have significant incentives to delay generic entry as long as possible.

1. Incentives to File Questionable Petitions

One way to delay generic entry is to suggest to the FDA that the generic drug is not safe or effective enough to enter the market. And typically, the mere filing of such a request—through a citizen petition—is enough to achieve the brand firm's goals. For while the FDA needs to examine the petition—and often the lengthy reports and studies that accompany it—it need not actually grant the petition for generic entry to be delayed. Even if the petition ultimately is denied, each day of

postponed competition could be worth millions of dollars to the brand firm.

Citizen petitions cost little for the companies that file them.¹²⁶ Consisting of boilerplate arguments, generally involving scientific data regarding a drug's manufacturing process, they are easy to file. Nor are there any consequences to filing frivolous petitions.¹²⁷ Questionable petitions create a backlog at the FDA, which in turn hinders the other administrative tasks the agency is charged with, such as approving ANDAs of other companies.¹²⁸

Just to pick one example, the FDA took seven years to respond to Aventis's 2003 petition against generic Lovenox, issuing a 45-page answer in 2010 that had to respond to not only the petition but also Aventis's 12 supplements and comments filed between 2004 and 2009.¹²⁹

"Eleventh hour" petitions, or petitions filed within six months of patent expiration, are particularly tempting as they force the FDA to take the time and resources to evaluate the merits of each filing, delaying generic approval.

Citizen petitions are more costly for generics, which are forced to invest resources in new studies, attempts to design around patents, and legal costs.¹³⁰ This process can be expensive, and if done too quickly, can compromise safety and efficacy of the drugs in dispute.

2. Role in Toolkit

Citizen petitions can also be used in combination with other activities to delay generic entry. For starters, parties often use these petitions to supplement "Paragraph IV" litigation. A generic company filing a Paragraph IV certification contends that the brand firm's patent is invalid or not infringed and that it should be allowed to enter the

¹²⁶ *Comment on Regulations: Making Your Voice Heard at FDA: How to Comment on Proposed Regulations and Submit Petitions*, *supra* note 43.

¹²⁷ *Generic Drug Maze Hearing*, *supra* note 41, at 70 (statement of Heather Bresch, Senior Vice President of Corporate Strategic Development, Mylan Laboratories, Inc.).

¹²⁸ *Id.* at 51 (statement of Gary Buehler, Director, Office of Generic Drugs, Food & Drug Admin.). In 1999, the FDA proposed a rule that would have separated the citizen petition process from the generic approval process but this was withdrawn in 2003. *Id.* at 61 (statement of Heather Bresch, Senior Vice President of Corporate Strategic Development, Mylan Laboratories, Inc.).

¹²⁹ FDA response to Aventis Pharmaceuticals Citizen Petition, Docket No. FDA-2003-P-0273 (Aug. 5, 2003), *available at* <http://www.regulations.gov/#!documentDetail;D=FDA-2003-P-0273-0002>.

¹³⁰ *Generic Drug Maze Hearing*, *supra* note 41, at 70 (statement of Heather Bresch, Senior Vice President of Corporate Strategic Development, Mylan Laboratories, Inc.).

market before the end of the patent term.¹³¹ The Hatch-Waxman Act grants the brand firm an automatic 30-month stay of FDA approval if it files an infringement lawsuit against the generic.¹³² Citizen petitions allow brand firms to obtain additional exclusivity beyond the 30-month stay. Petitions allow brand firms to keep generics off the market even if they lose their patent infringement lawsuits.

An example of this combination strategy is presented by the case of Biovail, which used a number of tactics to delay entry of a generic version of its best-selling anti-depression drug Wellbutrin XL. As discussed more fully below,¹³³ Biovail supplemented its strategy of initiating and settling infringement lawsuits with generics by filing a citizen petition with the FDA, which cost consumers \$37 million for each month the generic was delayed.¹³⁴

This example is not unique. In addition to the Wellbutrin, Ambien, and OxyContin cases discussed below,¹³⁵ Johnson & Johnson subsidiary Alza filed an eleventh-hour citizen petition in 2005 against Mylan, which planned to introduce a generic version of incontinence drug Ditropan XL.¹³⁶ Even though a court found less than 1 month later that Alza's patent was both invalid and not infringed, the brand was able to prevent generic competition for an additional 13 months, thereby receiving an extra \$1.8 million for each day that its petition blocked generic entry.¹³⁷

3. Relationship to Pending ANDAs

While the FDA is not required to respond to citizen petitions before the approval of any related ANDA, the result of such petitions is often a delay of the generic's entry.¹³⁸ Given its role in protecting public safety, the FDA naturally would be hesitant to approve an ANDA while a citizen petition is pending. It is no surprise, then, that many petitions

¹³¹ 21 U.S.C. § 355(j)(2)(A)(vii)(IV) (2006).

¹³² *Id.* § 355(j)(5)(B)(iii).

¹³³ See *infra* Section IV.A.

¹³⁴ *Meijer, Inc. v. Biovail Corp.*, Civil Action No. 08-2431, 2008 U.S. Dist. LEXIS 58135, at *6-7 (E.D. Pa. July 31, 2008); Marc Kaufman, *US: Petitions to FDA Sometimes Delay Generic Drugs: Critics Say Companies Misusing Process*, WASH. POST, July 3, 2006, at A1, available at <http://corpwatch.org/article.php?id=13827>.

¹³⁵ See *infra* Part V.

¹³⁶ *Generic Drug Maze Hearing*, *supra* note 41, at 60 (statement of Heather Bresch, Senior Vice President of Corporate Strategic Development, Mylan Laboratories, Inc.).

¹³⁷ Yael Waknine, *First-Time Generic Approvals: Ditropan XL, Zofran Injection/Premixed Injection, Oxandrin*, MEDSCAPE NEWS, Dec. 15, 2006, <http://www.medscape.com/viewarticle/549478>; Press Release, U.S. Senate Special Committee on Aging, Kohl, Leahy Introduce Bill To Stop Frivolous Citizen Petitions, Speed Generic Drug Approval (Sept. 28, 2006), available at <http://aging.senate.gov/record.cfm?id=268246>.

¹³⁸ *Generic Drug Maze Hearing*, *supra* note 41, at 69-70 (testimony of Heather Bresch, Senior Vice President of Corporate Strategic Development, Mylan Laboratories, Inc.).

are filed concerning pending ANDAs.

In fact, as shown in Table 2A in the Appendix, nearly half of brand petitions relate to bioequivalence or request additional studies. The FDA has shown concern with these petitions. It has explained that many petitions “contain[] data that had been available to the petitioner well before the date of the petition.”¹³⁹ And it has lamented that many petitions “involve[] theoretical arguments offered without full knowledge of the data actually submitted in the ANDAs.”¹⁴⁰

As a result, many of the petitions are “mixed decisions”: they are granted in part because the data requested is necessary, but they are denied in part because the petitioner has already included such data in the ANDA. Because of the theoretical nature of the “grant” and because the generic has already done what it is supposed to do, these are often effectively denials.

In cases involving citizen petitions and pending ANDAs, the FDA sometimes resolves the petition on the same day it grants the ANDA. One explanation for the confluence of these activities is the delay of ANDA approval until the agency resolves the petition.¹⁴¹

In fact, the FDA has noted the high correlation between citizen petitions and pending ANDAs, explaining that its own 2005 study showed that petitions were often filed shortly before anticipated ANDA approval.¹⁴² The agency found that 50% of petitions filed between 2004 and 2006 to block generic entry raised issues regarding bioequivalence “long after ANDA applicants ha[d] conducted their bioequivalence studies”¹⁴³

B. *Effect of 2007 Amendment*

In response to concerns presented by citizen petitions, Congress enacted the 2007 amendment to “stop frivolous petitions from delaying generic entry—and thus costing businesses, consumers, and taxpayers—by allowing needed competition to bring down prices in the pharmaceutical market.”¹⁴⁴

The new policy requires the FDA to respond to 505(q) petitions

¹³⁹ U.S. FOOD & DRUG ADMIN., REPORT TO CONGRESS: ENCOURAGING EARLY SUBMISSION OF CITIZEN PETITIONS AND PETITIONS FOR STAY OF AGENCY ACTION 3 (2009) [hereinafter FDA REPORT ENCOURAGING EARLY SUBMISSION], available at <http://www.hpm.com/pdf/FDA%202009%20505q%20CP%20Report%20to%20Congress.PDF>.

¹⁴⁰ *Id.*

¹⁴¹ Seth C. Silber et al., *Abuse of the FDA Citizen Petition Process: Ripe for Antitrust Challenge?*, 25 ANTITRUST HEALTH CARE CHRON. 26, 39 (2012).

¹⁴² FDA REPORT ENCOURAGING EARLY SUBMISSION, *supra* note 139, at 3.

¹⁴³ *Id.* at 4.

¹⁴⁴ 153 CONG. REC. 10,924 (2007) (statement of Sen. Debbie Stabenow).

within 180 days of a petition's submission.¹⁴⁵ The agency can delay its approval of an ANDA while a petition is pending only if the delay is "necessary to protect the public health."¹⁴⁶

Despite these objectives and requirements, the figures above show that the amendment has not been successful in reducing the number of citizen petitions. The data actually show an increase in petitions following the amendment. In the three years after the passage of the amendment, there were an average of 34 filings a year, as compared with 27 per year in the three years before the amendment.¹⁴⁷ In addition, the number of brand petitions against generics increased from 9 to 16 each year. And brands' success rate against generics declined marginally from an average of 20% in the three years before the amendment to 19% in the three years after its enactment.¹⁴⁸

Pursuant to the 2007 amendment, the FDA is required to file a report with Congress on its success in expeditiously responding to section 505 petitions. In its 2010 report, the FDA stated that "additional experience and trend data" were needed "to determine whether section 505(q) is accomplishing the stated goals of the legislation."¹⁴⁹ But the agency acknowledged that the amendment "may not be discouraging the submission of petitions that do not raise valid scientific issues and are intended primarily to delay the approval of competitive drug products."¹⁵⁰ The FDA also "believe[d] that innovator companies may be implementing strategies to file serial 505(q) petitions and petitions for reconsideration in an effort to delay approval of ANDAs or 505(b)(2) applications for competing drugs."¹⁵¹

On January 3, 2012, the FDA proposed for notice and comment an amendment that would make changes to section 505(q). In particular, it would require all data, even unfavorable data, to be included in a petition. It would require the petitioner to include the exact date information relevant to the petition became known to it. And it would make clear that the FDA has the authority to dismiss certain petitions and label them as "moot."¹⁵²

It is unclear if these changes will reduce the number of petitions granted or increase their success rate. But what is clear is that the 2007 amendment has not been successful in achieving its stated purposes.

¹⁴⁵ 21 U.S.C. § 355(q)(1)(F) (2006); GUIDANCE FOR INDUSTRY, *supra* note 68, at 3.

¹⁴⁶ 21 U.S.C. § 355(q)(1)(A)(ii); *see also* GUIDANCE FOR INDUSTRY, *supra* note 68, at 2 (quoting 21 U.S.C. § 355(q)(1)(A)).

¹⁴⁷ *See supra* Table 1.

¹⁴⁸ *See supra* Figure 2 and notes 117, 118.

¹⁴⁹ 2010 FDA REPORT, *supra* note 104, at 5.

¹⁵⁰ *Id.*

¹⁵¹ *Id.*

¹⁵² Alexander Gaffney, *Proposed FDA Rule Would Amend Citizen Petition Regulations*, REG. FOCUS, Jan. 3, 2012, <http://www.raps.org/focus-online/news/news-article-view/article/563/proposed-fda-rule-would-amend-citizen-petition-regulations.aspx>.

While the FDA is awaiting additional experience and data regarding the success of the amendment, this Article has shown that, to date, the amendment has not reduced the number of unsuccessful (in other words, denied or essentially denied) citizen petitions that appear to be filed to delay generic competition.

V. EXAMPLES

The concerns mentioned above are not hypothetical. This Part introduces three examples that demonstrate the delay that brand firms can attain by filing questionable citizen petitions. It analyzes the examples of depression drug Wellbutrin XL, insomnia drug Ambien CR, and pain-reliever OxyContin.

A. *Wellbutrin XL*

The first example is provided by the drug Wellbutrin XL, an extended-release drug developed by Biovail to treat depression and prevent seasonal affective disorder (SAD).¹⁵³ Wellbutrin entered the market in 2004 with annual sales of nearly \$1 billion.¹⁵⁴

Also in 2004, four generics filed ANDAs to enter the market with a generic version of bupropion hydrochloride, the active ingredient in Wellbutrin XL. Each filed a Paragraph IV certification and claimed it would not infringe Biovail's patents.¹⁵⁵ Biovail then sued two of the four generics, Anchen and Abrika, for patent infringement. This suit, in December 2004, triggered a 30-month stay of ANDA approval under the Hatch-Waxman Act.¹⁵⁶ In November 2005, the FDA tentatively granted Anchen's ANDA for a generic version of Wellbutrin XL. Because of the 30-month stay, however, Anchen could not enter the

¹⁵³ Kristi Monson & Arthur Schoenstadt, *Wellbutrin XL*, EMEDTV, <http://depression.emedtv.com/wellbutrin-xl/wellbutrin-xl.html> (last updated Dec. 19, 2011).

¹⁵⁴ *Top 200 Prescribed Drugs by Sales in 2004*, DRUGS.COM, http://www.drugs.com/top200_2004.html [hereinafter *Top 200 Drugs by Sales 2004*] (last visited Aug. 25, 2012).

¹⁵⁵ The relevant patents are U.S. Patent Nos. 6,096,341 & 6,143,327. *In re Wellbutrin XL Antitrust Litigation*, Civil Action No. 08-2431, 2009 WL 678631, at *2 (E.D. Pa. 2009). The ANDAs were filed on September 21, 2004 by Anchen Pharmaceuticals, September 23, 2004 by Abrika Pharmaceuticals, November 30, 2004 by Impax Laboratories, and July 21, 2005 by Watson Pharmaceuticals. FDA Response to Biovail Corporation Citizen Petition, Docket No. FDA-2005-P-0366, at 2 n.3 (Dec 14, 2006) [hereinafter FDA Response to Biovail], available at <http://www.regulations.gov/#!documentDetail;D=FDA-2005-P-0366-0004> (originally Docket No. FDA-2005-P-0498).

¹⁵⁶ *In re Wellbutrin XL Antitrust Litigation*, 260 F.R.D. 143, 150 (E.D. Pa. 2009). Biovail later filed patent infringement suits against the other two ANDA filers, Impax and Watson. *Id.* at 150–51.

market.¹⁵⁷

On December 20, 2005, Biovail submitted a citizen petition requesting that the FDA not approve any ANDAs for generic versions of Wellbutrin XL.¹⁵⁸ The petition requested that all ANDAs undergo additional bioequivalence studies before approval and claimed the studies were needed to prevent seizures and ascertain the drug's effects when taken with alcohol.¹⁵⁹ The petition requested that ANDAs prove bioequivalence to not only Wellbutrin XL, but also the previous version of the drug, sustained-release Wellbutrin SR.¹⁶⁰

On August 1, 2006, a district court found that Anchen did not infringe Biovail's patent.¹⁶¹ This finding of noninfringement ended Biovail's 30-month stay of FDA. But Biovail's pending citizen petition meant that the FDA still could not allow any generic versions of Wellbutrin XL to enter the market.

Four months later, on December 14, 2006, the FDA responded to Biovail's citizen petition.¹⁶² Formally, the petition was granted in part and denied in part.¹⁶³ But a closer analysis reveals that the FDA essentially denied the petition. The agency denied the petition on the grounds that ANDAs only had to prove bioequivalence to Wellbutrin XL (not all versions of Wellbutrin), and that Biovail failed to offer evidence showing that other requested studies were needed.¹⁶⁴

On the other hand, the agency "granted" Biovail's request for certain bioequivalence studies on the grounds that such studies were already requirements of the FDA's approval process for such drugs.¹⁶⁵ In other words, Biovail's request for studies was granted but had no effect since the agency required the studies anyway. Similarly granted was Biovail's request for certain "dose dumping" information,¹⁶⁶ which the FDA already required from ANDA applicants.¹⁶⁷

In addition, the FDA's response made it clear that brands did not have "the right to be free of generic competition" and that "Biovail [should] not be permitted to shield its market share."¹⁶⁸

On December 14, 2006, the same day the FDA responded to

¹⁵⁷ *Id.* at 150.

¹⁵⁸ *Id.* at 151; Biovail Citizen Petition, Docket. No. 2005P-0498/CP1 (Dec. 20, 2005), available at <http://www.fda.gov/ohrms/dockets/dockets/05p0498/05p-0498-cp00001-toc.htm>.

¹⁵⁹ Biovail Citizen Petition, *supra* note 158, at 4.

¹⁶⁰ *Id.*

¹⁶¹ Biovail Labs. v. Anchen Pharm., 463 F. Supp. 2d 1073, 1077-78 (C.D. Cal. 2006).

¹⁶² FDA Response to Biovail, *supra* note 155.

¹⁶³ *Id.* at 2.

¹⁶⁴ *Id.* at 18.

¹⁶⁵ *Id.*

¹⁶⁶ "Dose dumping" refers to the release of a drug faster than expected. ACS News Service Weekly PressPac—Medicinal Products Susceptible to 'Dose Dumping' Should Be Fully Tested, ACS.ORG (Sept. 23, 2009), <http://www.physorg.com/news172934081.html>.

¹⁶⁷ FDA Response to Biovail, *supra* note 155, at 18.

¹⁶⁸ *Id.* at 16; see Silber et al., *supra* note 141, at 36.

Biovail's petition, the agency approved the first generic version of Wellbutrin XL, filed by Anchen Pharmaceuticals.¹⁶⁹

Even though the FDA effectively denied the petition, Biovail had taken advantage of its time on the market without generic competition, becoming one of the top 20 drugs on the market in 2006 with total U.S. sales of more than \$1.6 billion.¹⁷⁰ In the 133 days between the lifting of Biovail's 30-month stay on August 1, 2006 and the FDA response to Biovail's petition on December 14, 2006, Wellbutrin XL enjoyed sales of more than \$600 million.¹⁷¹

Once generics entered the market, of course, Biovail's sales plummeted. In 2007, Wellbutrin XL suffered a decline of more than 40% in sales, grossing less than \$1 billion.¹⁷² In the next two years, sales declined to roughly \$600 million and \$200 million,¹⁷³ with less than 1 million units sold in 2009.¹⁷⁴

In short, the extra 133 days of delay that Biovail obtained by filing a citizen petition allowed it to gain an additional \$600 million, even after a court had ruled that the generic drug did not infringe its patent.

B. *Ambien*

The second example is provided by the insomnia drug Ambien.¹⁷⁵ In September 2005, the FDA approved Ambien CR, a controlled-release version of its best-selling drug Ambien IR (immediate release).¹⁷⁶ The time-release formula offered by Ambien CR improved on the previous version, which frequently did not allow patients to achieve seven or eight hours of sleep.

In January 2006, Anchen Pharmaceuticals filed the first Paragraph

¹⁶⁹ Letter from Gary Buehler, Director, Office of Generic Drugs, to Anchen Pharmaceuticals, (Dec. 14, 2006), available at http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2006/077284s000ltr.pdf.

¹⁷⁰ *Top 200 Prescribed Drugs by Sales in 2006*, DRUGS.COM, http://www.drugs.com/top200_2006.html [hereinafter *Top 200 Drugs by Sales 2006*] (last visited Feb. 15, 2012).

¹⁷¹ *Id.* (apportioning 2006 sales of \$1,670,516 for the 133 days of delay).

¹⁷² *Top 200 Prescribed Drugs by Sales in 2007*, DRUGS.COM, http://www.drugs.com/top200_2007.html [hereinafter *Top 200 Drugs by Sales 2007*] (last visited July 8, 2012).

¹⁷³ *Top 200 Prescribed Drugs by Sales in 2008*, DRUGS.COM, http://www.drugs.com/top200_2008.html [hereinafter *Top 200 Drugs by Sales 2008*] (last visited July 8, 2012); *Top 200 Prescribed Drugs by Sales in 2009*, DRUGS.COM, http://www.drugs.com/top200_2009.html [hereinafter *Top 200 Drugs by Sales 2009*] (last visited Feb. 15, 2012).

¹⁷⁴ *Top 200 Drugs by Units Sold (2009)*, DRUGS.COM, http://www.drugs.com/top200_units_2009.html (last visited Feb. 15, 2012).

¹⁷⁵ FDA Response to Sanofi-Aventis Citizen Petition, Docket No. FDA-2007-P-0182, at 2 (Oct. 13, 2010) [hereinafter FDA Response to Sanofi-Aventis], available at <http://www.regulations.gov/#!documentDetail;D=FDA-2007-P-0182-0017> (originally Docket No. 2007-P-0224).

¹⁷⁶ *Id.*; Sanofi-Aventis SA (SNY), WIKINVEST, http://www.wikinvest.com/stock/Sanofi-Aventis_SA_%28SNY%29/Stilnox_Ambien_Myslee (last visited Aug. 9, 2012).

IV certification, seeking to enter the market with a generic version of Ambien CR.¹⁷⁷ Upon receiving notification of the certification, Sanofi decided not to sue Anchen, which meant that it did not receive a 30-month stay of FDA approval.

On June 7, 2007, before the FDA took any action on Anchen's ANDA, Sanofi filed a citizen petition requesting that the agency "take special consideration when reviewing any [ANDA] for a generic version of the extended-release (ER) formulation of Ambien."¹⁷⁸ The petition requested that the FDA require ANDA applicants to provide specific bioequivalence data "in addition to traditional bioequivalence parameters" by demonstrating therapeutic equivalence to both Ambien IR and Ambien CR.¹⁷⁹

The FDA finally responded to Sanofi's petition on October 13, 2010, more than three years—1,225 days to be precise—after Sanofi's petition. The FDA stated that the petition was granted in part and denied in part, but a more careful analysis shows that the agency essentially denied the petition. The FDA "granted" the petition to the extent it promised to carefully evaluate studies submitted by future ANDA applicants. But as applied to the petition under review, it denied the petition, finding that Anchen would not need to conduct additional studies.¹⁸⁰

In December 2010, two months after the FDA responded to the petition, it approved Anchen's generic version of Ambien CR.¹⁸¹ In the period between Sanofi's filing of the petition on June 7, 2007 and the FDA's ruling on the petition on October 13, 2010, Sanofi gained at least \$850 million in sales each year. The 1,225-day delay resulting from the petition allowed Sanofi to amass more than \$3.1 billion in sales.¹⁸²

C. *OxyContin*

Purdue Pharma's pain medication OxyContin provides the third example of a delay in generic entry resulting from the filing of a citizen

¹⁷⁷ *Drugs@FDA*, *supra* note 100; CHIH-MING CHEN, ANCHEN PHARMACEUTICALS, INC.: ITS PAST AND ITS FUTURE 8 (2007), available at <http://rx.mc.ntu.edu.tw/alumni/epaper/16/01.pdf>.

¹⁷⁸ FDA Response to Sanofi-Aventis, *supra* note 175, at 1 (footnote omitted).

¹⁷⁹ *Id.*

¹⁸⁰ *Id.* at 12.

¹⁸¹ *Par to Acquire Anchen Pharmaceuticals*, PHARMACEUTICAL NEWS (Sept. 26, 2011, 8:24 AM), <http://thepharmaceutical-news.com/par-to-acquire-anchen-pharmaceuticals>.

¹⁸² *Top 200 Drugs by Sales 2007*, *supra* note 172 (noting 2007's \$522 million in sales based on 207 days—Jan. 1, 2007 to June 7, 2007—of \$920 million annual sales); *Top 200 Drugs by Sales 2008*, *supra* note 173 (noting 2008's \$865 million in annual sales); *Top 200 Drugs by Sales 2009*, *supra* note 173 (noting 2009's \$983 million in annual sales); *Top 200 Prescribed Drugs by Sales in 2010*, DRUGS.COM, http://www.drugs.com/top200_2010.html [hereinafter *Top 200 Drugs by Sales 2010*] (last visited Feb. 15, 2012) (calculating Sanofi's 2010 sales to be \$742 million based on 285 days—Jan. 1, 2010 to Oct. 13, 2010—of \$950 million annual sales).

petition. Although the drug's active ingredient, oxycodone, was developed nearly a century ago, Purdue's controlled-release version, which releases the drug over time, gained FDA approval in 1995.¹⁸³

OxyContin was a blockbuster drug. In the early 2000s, it consistently grossed more than \$1 billion per year in sales, reaching \$1.8 billion in 2003.¹⁸⁴ On January 6, 2004, Purdue filed a stay of action petition, a request for the FDA to refrain from approving any additional ANDAs for oxycodone.¹⁸⁵ Purdue asked the FDA to require all ANDA applicants to implement a risk-management program¹⁸⁶ prior to marketing the drug and to include certain labeling information.¹⁸⁷ The FDA denied the petition on March 23, 2004.¹⁸⁸

That very day, the issue was rendered moot by the FDA's approval of two ANDAs for oxycodone hydrochloride controlled-release tablets submitted by generic companies Endo and Teva.¹⁸⁹ After the generics entered the market, Purdue's OxyContin sales fell for the next three years, reaching \$680 million in 2006.¹⁹⁰

In 2006, the Federal Circuit overturned a lower court judgment, finding that ANDA filers Endo and Teva had infringed Purdue's patent covering the controlled-release oxycodone drug.¹⁹¹ As a result, the generics left the market, and OxyContin then attained sales in excess of \$1 billion.¹⁹²

On June 7, 2007, three years after the FDA approved oxycodone ANDAs, Purdue filed a citizen petition with the FDA, requesting that the FDA refrain from approving any NDAs or ANDAs for oxycodone hydrochloride products containing certain ingredients until the agency (1) adopted industry standards consistent with the safety standards and studies required of Purdue and (2) formally withdrew the denial of

¹⁸³ FDA Response to Purdue Pharma L.P. Citizen Petition, Docket No. FDA-2007-P-0245, at 2 (Nov. 15, 2011) [hereinafter FDA Response to Purdue Pharma], available at <http://www.regulations.gov/#!documentDetail;D=FDA-2007-P-0245-0005> (originally FDA-2004-P-0232).

¹⁸⁴ *Top 200 Prescribed Drugs by Sales in 2003*, DRUGS.COM, http://www.drugs.com/top200_2003.html (last visited July 8, 2012).

¹⁸⁵ FDA Response to Purdue Pharma, *supra* note 183, at 1.

¹⁸⁶ Risk management programs are programs a company implements to comply with government regulations and maintain safety. Such programs typically include elements such as clear labels for patients and doctors, comprehensive educational programs, as well as surveillance and intervention for "misuse, abuse, addiction, diversion, and overdose and other related serious adverse events." FDA Response to Purdue Pharma L.P. Petition for Stay of Action, Docket No. FDA-2004-P-0006, at 2-3 (Mar. 23, 2004) [hereinafter FDA Response to Purdue Pharma's Stay], available at <http://www.regulations.gov/#!documentDetail;D=FDA-2004-P-0473-0002>.

¹⁸⁷ FDA Response to Purdue Pharma, *supra* note 183, at 2.

¹⁸⁸ FDA Response to Purdue Pharma's Stay, *supra* note 186, at 1.

¹⁸⁹ *Id.* at 2.

¹⁹⁰ *Top 200 Drugs by Sales 2006*, *supra* note 170.

¹⁹¹ *Purdue Pharma L.P. v. Endo Pharm., Inc.*, 438 F.3d 1123, 1126 (Fed. Cir. 2006).

¹⁹² *Top 200 Drugs by Sales 2008*, *supra* note 173.

Purdue's early petition for stay.¹⁹³

Because there were no pending ANDAs or NDAs, the FDA was not bound by the 180-day deadline under section 505(q). The agency did not respond to the petition until March 2008, ultimately denying Purdue's petition on the grounds that the FDA applies consistent guidelines for product approval and that it was unnecessary to adopt Purdue's requested standards.¹⁹⁴

Purdue's petition requested safety standards that had been satisfied three years earlier at the time Endo's and Teva's ANDAs were approved. Even if the generics were removed from the market because they infringed Purdue's patent, there was no question that the drugs were safe and effective.

CONCLUSION

Citizen petitions have received far less attention than other conduct in the pharmaceutical industry, such as settlements between brand and generic companies and product hopping. But they have played a pivotal role in delaying generic entry. Attention to the roadblocks they have erected against generic competition is needed.

After studying every petition filed between 2001 and 2010, this Article concludes that petitions have increased in the past decade. Brand firms file most (68%) of the petitions, with more than 75% of these targeting generic drugs. And the FDA denies the vast majority (81%), granting only 19% of the petitions.

The study finds that, while all categories of petitions confront denial more than success, generic filers are more successful than brands, with 28% grant and 72% denial rates, as compared to 19% grant and 81% denial rates for brand filers.

The study also finds that Congress's 2007 legislation has not been successful in reducing the number of petitions. After passage of the amendment, the number of filings increased from 27 to 34 per year, with brand petitions against generics increasing from 9 to 16 per year.

Citizen petitions are an essential tool in the toolbox that brand companies have used to prolong their monopoly on the market. In short, and in defiance of Congress's attempt to limit abuse, citizen petitions play an increasingly important role in delaying generic competition.

¹⁹³ FDA Response to Purdue Pharma, *supra* note 183, at 2.

¹⁹⁴ *Top 200 Drugs by Sales 2010*, *supra* note 182 (noting OxyContin's 2010 total sales of \$3.55 billion).

APPENDIX

Table 1A
Breakdown of Mixed Decisions

	Essentially Granted		Essentially Denied		Remains Mixed Decision	
2001	1	33%	1	33%	1	33%
2002	1	20%	1	20%	3	60%
2003	0	0%	1	100%	0	0%
2004	1	25%	3	75%	0	0%
2005	1	25%	3	75%	0	0%
2006	0	0%	3	50%	3	50%
2007	3	50%	2	33%	1	17%
2008	1	33%	2	67%	0	0%
2009	1	11%	5	56%	3	33%
2010	3	30%	2	20%	5	50%
Total	12	24%	23	45%	16	31%

Table 2A
Categories of Brand Challenges

	Safety		Bioequiv- alence		Additional Studies		Labels		Other	
2001	1	33%	2	67%	0	0%	0	0%	0	0%
2002	3	43%	0	0%	0	0%	1	14%	3	43%
2003	2	13%	4	25%	2	13%	2	13%	6	38%
2004	4	15%	7	26%	8	30%	0	0%	8	30%
2005	1	7%	7	47%	2	13%	1	7%	4	27%
2006	3	12%	7	28%	1	4%	2	8%	12	48%
2007	3	14%	3	14%	5	24%	2	10%	8	38%
2008	6	21%	6	21%	8	31%	4	12%	4	14%
2009	2	6%	10	31%	9	28%	1	3%	10	31%
2010	0	0%	7	47%	3	20%	1	6%	4	27%
Total	25	13%	53	28%	38	20%	14	7%	59	31%

Figure 1A
Original Success Rate of Citizen Petitions

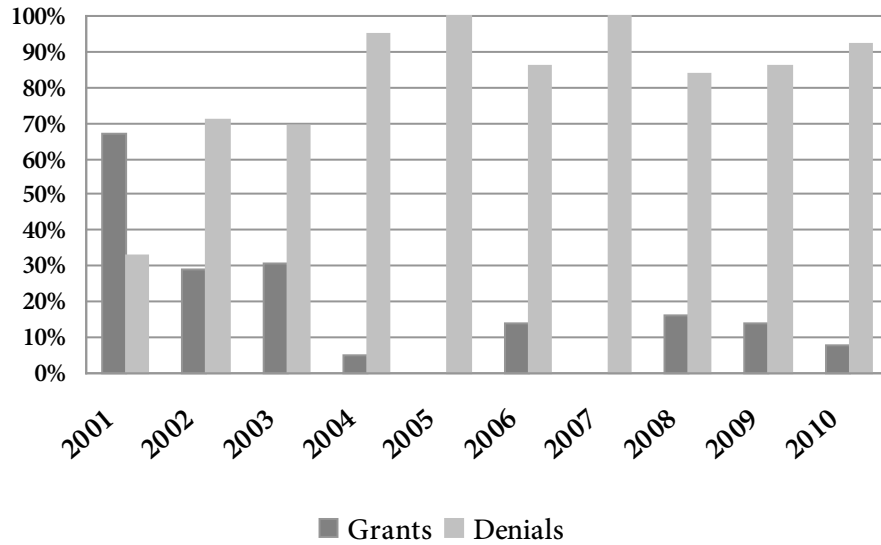


Table 3A
Original Success Rate of Citizen Petitions

	Granted		Denied		Total
2001	4	67%	2	33%	6
2002	2	29%	5	71%	7
2003	4	31%	9	69%	13
2004	1	5%	18	95%	19
2005	0	0%	9	100%	9
2006	1	14%	6	86%	7
2007	0	0%	13	100%	13
2008	3	16%	16	84%	19
2009	3	14%	18	86%	21
2010	1	8%	11	92%	12
Total	19	15%	107	85%	126

Figure 2A
Original Brand Win Rate



Figure 2A is similar to Figure 2 presented above. It differs by taking the FDA's grants and denials at face value. In other words, it does not parse the mixed decisions to determine if they are effectively grants or denials.

The data accompanying Figure 2A show that the FDA granted brand petitions 11 times (8%), denied them 78 times (60%), and reached mixed decisions in 41 (32%) cases.¹⁹⁵ Focusing only on the cases in which the FDA granted and denied brand petitions, there were 12% grants and 88% denials. As the data reveal, generics encountered more success than brand firms. There were 8 grants (24%), 19 denials (58%), and 6 mixed (18%) cases.¹⁹⁶

Figure 3A
Original Brand Win Rate Against Generics

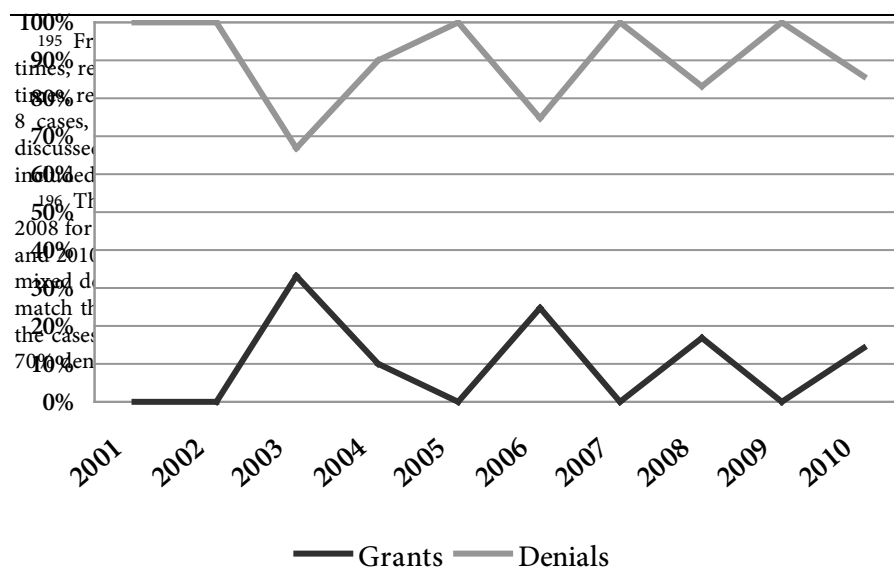


Figure 3A is similar to Figure 3 presented above. Like Figure 2A, it differs by taking the FDA's grants and denials at face value. The FDA granted brand petitions against generics 7 times (7%), denied them 58 times (58%), and reached mixed decisions in 35 (35%) cases.¹⁹⁷ Focusing only on the cases in which the FDA granted and denied petitions, there were 11% grants and 89% denials.

Brand petitions against other brands were more successful. The agency granted these petitions 3 times and denied them 5 times.¹⁹⁸

¹⁹⁷ The FDA granted 2 brand petitions against generics in 2003 and 2008, and 1 each in 2004, 2006, and 2010, for a total of 7. It denied 58 petitions (from 2001 through 2010: 1, 3, 4, 9, 4, 3, 6, 10, 12, and 6). And it reached mixed results in 35 cases (2, 1, 1, 1, 4, 5, 5, 3, 5, and 8).

¹⁹⁸ The FDA granted 3 brand petitions against brands (1 in 2002 and 2 in 2003), and it denied 5 (3 in 2003 and 2 in 2007).