

CITIZEN PETITIONS: AN EMPIRICAL STUDY

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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 3/4 of brand petitions targeting generic drugs.

The study concludes that the FDA has granted 19% of citizen petitions and 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 by 68% (from 9 to 16 per year). And the grant rate for brands’ 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 used more frequently and that has evaded attempts to limit its abusive potential, citizen petitions warrant scrutiny.

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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 have paid 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 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.

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 2007, in response to the hearing, and because of congressional legislation, the FDA changed its rules on petitions, promising to respond within 180 days. But despite this attention, 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 the targets of the petitions are, 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 have been filed after the 2007 legislation that was supposed 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 brand petitions, more than 3/4 target generic entrants.

The study concludes that the FDA has granted 19% of petitions and denied 81%. It also observes that generics' petitions are more successful, with 28% granted and 72% denied, as compared to brands, 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 by 68% (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

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

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 (*e.g.*, tablet) to another (*e.g.*, capsule). 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, and requirements of petitions. It also raises some concerns with petitions that government officials have articulated. Finally, it 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, it 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 – that they are filed not because of actual concerns with 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 of the 2007 amendment 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, 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 was no generic equivalent for roughly 150 drugs whose patent term had lapsed.⁶

In the Act, Congress employed several mechanisms to promote generic competition. First, it allowed generics to experiment on drugs during the patent term.⁷ Second, the legislature created a new process for obtaining FDA approval. The Act recognized a new type of drug application, called an Abbreviated New Drug Application (ANDA), that allowed generics to rely on brands' safety and effectiveness 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

² Drug Price Competition and Patent Term Restoration Act of 1984, 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 U.S. Dep't of Health & Human Servs., Food & Drug Admin., Center for Drug Eval. & Research, *Generic Drugs: Questions and Answers* (2007), http://www.fda.gov/buyonlineguide/generics_q&a.htm.

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

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

⁷ 35 U.S.C. § 271(e)(1)(2004) (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 Federal Trade Commission, *Generic Drug Entry Prior to Patent Expiration: An FTC Study*, at 5, <http://www.ftc.gov/os/2002/07/genericdrugstudy.pdf> [hereinafter Generic Drug Study].

enter during the patent term.⁹ During the period, which begins after the first commercial 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, the brand loses 45 to 90% of its market share within the first twelve months.¹⁸ Generic entry is most likely in large markets, especially with blockbuster products, but occurs with respect to drugs of many

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

¹⁰ Generic Drug Study, *supra* note 8, at 7. Until amended in 2003, the Hatch-Waxman Act included as a second trigger for the 180-day period a court decision finding invalidity or lack of infringement.

¹¹ See Kathleen D. Jaeger, President & CEO, Generic Pharm. Ass'n, Testimony Before the H.R. Comm. on Energy and Commerce, Oct. 9, 2002, available at <http://www.gphaonline.org/resources/2002/10/08/greater-access-affordable-pharmaceuticals-act>.

¹² IMS Institute for Healthcare Informatics, *The Use of Medicines in the United States: Review of 2010* (2011).

¹³ CBO STUDY, *supra* note 5, at 37.

¹⁴ *Id.* at xiii; Ctr. for Drug Eval. & Research, FDA, Generic Competition and Drug Prices (2006), http://www.fda.gov/CDER/ogd/generic_competition.htm.

¹⁵ CBO STUDY, *supra* note 5, at xiii.

¹⁶ *See id.*

¹⁷ Ctr. for Drug Eval. & Research, FDA, *Savings from Generic Drugs Purchased at Retail Pharmacies* (2004), <http://www.fda.gov/cder/consumerinfo/savingsfromgenericdrugs.htm>.

¹⁸ CBO STUDY, *supra* note 5, at xiii; Doug Long (IMS), *2003 Year in Review: Trends, Issues, Forecasts*, at 35 (2004) (on file with author); Atanu Saha et al., *Generic Competition in the U.S. Pharmaceutical Industry*, 13 INT. J. ECON. BUS. 15, 31 (2006).

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

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 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

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).

²⁵ These agreements are called reverse payments since they differ from typical licensing payments that flow from challengers to patentees.

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 that 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 QUART. J. 1, 20 (2006).

Another type of activity in the pharmaceutical industry that has raised 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 to consumers. These laws allow (and in some cases 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 by brand firms’ product hopping. Switching to a new version of the drug prevents a pharmacist from substituting a generic version because the generic is not equivalent to the brand version.³³

E. Timing

A central issue in both settlements and product hopping involves timing. Product hopping is most successful when brand firms can not only avoid state DPS laws but also 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

²⁸ Keith 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 DRUG PRODUCT SELECTION, STAFF REPORT TO THE FTC 2-3 (Jan. 1979).

³² Doctors are subject to a vast array of drug promotion, which includes detailing (sales calls to doctor’s 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. STUART O. SCHWEITZER, *PHARMACEUTICAL ECONOMICS AND POLICY* 87-93 (2d ed. 2007); A. MASSON & R. STEINER, *GENERIC SUBSTITUTION AND PRESCRIPTION DRUG PRICES: ECONOMIC EFFECTS OF STATE DRUG PRODUCT SELECTION LAWS* 7 (1985).

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

³⁴ *Id.* at 49.

³⁵ *Id.* at 51-55.

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.

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

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 effectiveness – 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 effective 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 the parties that 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.

³⁶ EUROPEAN COMMISSION, PHARMACEUTICAL SECTOR INQUIRY FINAL REPORT, ¶¶ 3, 1010 http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/staff_working_paper_part1.pdf.

³⁷ *Id.* ¶ 1028.

A. Introduction

U.S. citizens have a right under the First Amendment to petition the government to act.³⁸ 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.³⁹ The FDA allows individuals to express “general concerns about safe, scientific, or legal issues regarding a product any time before its market entry.”⁴⁰

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.”⁴¹

All citizen petitions must include the “action requested,” in particular, the “rule, order, or other administrative action” that the petitioner seeks to “issue, amend or revoke.”⁴² They also must disclose a “[s]tatement of grounds,” including “the factual and legal grounds for the petition.”⁴³

Citizen petitions must describe any environmental effects.⁴⁴ 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.”⁴⁵

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

Second, generics file petitions to obtain the FDA’s approval so they can

³⁸ U.S. CONST. art. I (“Congress shall make no law...abridging the freedom...to petition the Government for a redress of grievances.”).

³⁹ Administrative Procedure Act, 5 U.S.C. § 553(e) (2010); *see generally* Stacey B. Lee, *Is a Cure on the Way?*, 20 KAN. J.L. & PUB. POL’Y 98, 109 (2010).

⁴⁰ 21 C.F.R. § 10.30(a) (2010); *The Generic Drug Maze: Speeding Access to Affordable Life-Saving Drugs: Hearing Before the Sen. Sp. Comm. on Aging*, 109th Cong. 2d Sess. 6 (2006) (statement of Senator Herb Kohl) [hereinafter *Generic Drug Maze hearing*]. *See also* 21 C.F.R. § 10.30(b)(B) (requiring petitions to state factual and legal grounds for requests).

⁴¹ 21 C.F.R. §§ 10.25, 10.30.

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

⁴³ 21 C.F.R. § 10.30(b).

⁴⁴ *Id.* § 10.30(b)(C).

⁴⁵ *Id.* § 10.30(b)(D).

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 or 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 as aware of this issue as anyone. In 2006 testimony in a Senate hearing about citizen petitions, Director Gary Buehler explained that “[i]t is very rare that petitions present new issues that CDER has not fully considered.”⁴⁶ In fact, even if the petition process could be valuable in theory, “very few of these petitions on generic drug matters have presented data or analysis that significantly altered FDA’s policies.”⁴⁷ Despite this, “the Agency must nevertheless assure itself of that fact by reviewing the citizen petitions.”⁴⁸

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 review arguments that could have been previously made.⁴⁹

Director Buehler noted that, of the 42 FDA responses to citizen petitions filed between 2001 through 2005, the agency denied 33, denied 3 in part, and granted 6.⁵⁰ Even these figures overstated the petitions’ contribution. 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.”⁵¹

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

⁴⁶ *Generic Drug Maze hearing*, *supra* note 40, at 15 (statement of Gary Buehler, Director, Office of Generic Drugs, Center for Drug Evaluation and Research, Food and Drug Administration).

⁴⁷ *Id.*

⁴⁸ *Id.*

⁴⁹ Marc Kaufman, *Petitions to FDA Sometimes Delay Generic Drugs*, WASH. POST., at A1, July 3, 2006.

⁵⁰ *Id.*

⁵¹ *Id.* For a fuller discussion of this issue, see *infra* notes 82-97 and accompanying text.

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 its industry guidelines outlining what is generally suggested to achieve FDA approval.

Just 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.⁵² The petition requested that “all bioequivalence studies be performed under both fed and fasting conditions.”⁵³ The FDA “granted in part” the request “[b]ecause we expect generic applicants to measure [the active ingredients] in both fed and fasting studies.”⁵⁴ 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.⁵⁵ The petition nonetheless delayed generic entry, with the FDA taking more than 14 months to file a substantive response.⁵⁶

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.⁵⁷ 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.”⁵⁸ Additionally, the CDER conducts a “thorough legal review” since petitioners often “submit non-scientific petitions that raise purely legal questions related to ANDA approvals.”⁵⁹ For years, this array of challenges contributed to a backlog at the FDA.

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.⁶⁰ In other

⁵² *FDA Response to Ortho-McNeil Pharmaceuticals, Inc. Citizen Petition*, Dkt. No. FDA-2005-P-0002, at 1, <http://www.regulations.gov#!documentDetail;D=FDA-2005-P-0002-0002> (last visited Feb. 15, 2012) [*hereinafter* *FDA Response to Ortho-McNeil*].

⁵³ *Id.*

⁵⁴ *Id.*

⁵⁵ *Id.* at 6. For further discussion of this issue, see *infra* notes 82-97 and accompanying text.

⁵⁶ *Id.* at 1.

⁵⁷ *Generic Drug Maze hearing*, *supra* note 40, at 14 (statement of Gary Buehler); see also 21 C.F.R. § 10.30(E) (“The Commissioner shall . . . rule on each petition filed . . . [and] shall furnish a response to each petitioner within 180 days of receipt of the petition.”).

⁵⁸ *Generic Drug Maze hearing*, *supra* note 40, at 14 (statement of Gary Buehler).

⁵⁹ *Id.*

⁶⁰ 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”).*Id.*

words, it often took the FDA longer than the 6-month time frame to reach a final decision. Just to give one example, Aventis filed a petition in 2003 concerning Lovenox, a drug preventing blood clots. The FDA did not reach a final decision until 2010, a total of 2,644 days after the petition was first filed.⁶¹

Congress held hearings in 2006 on citizen petitions and delays in the process. Testifying from government were Gary Buehler and Jon Leibowitz, then-Commissioner (and subsequently Chairman) of the Federal Trade Commission. From private industry were Heather Bresch, senior vice president at Mylan Laboratories, and Mark Merritt, president and CEO of Pharmaceutical Care Management Association.⁶² Each highlighted concerns presented by citizen petitions.

C. 2007 amendment

As a result of the 2006 hearing,⁶³ Congress enacted Section 914 of Title IX of the Food and Drug Administration Amendments Act (FDAAA) of 2007,⁶⁴ which added a new rule, known as section 505(q), to citizen petitions.⁶⁵ The legislature sought to ensure that the FDA did not delay approval of drug applications unless a petition was “necessary to protect public health.”⁶⁶ 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.”⁶⁷

Section 505(q) applies to “certain petitions that request that FDA take any form of action related to a pending ANDA.”⁶⁸ It also requires petitioners to

⁶¹ Although the petition was granted in part and denied in part, it essentially was denied since the FDA concluded that Aventis’ requests for additional bioequivalence studies were unnecessary. *FDA Response to Aventis Pharmaceuticals, Inc. Citizen Petition*, Dkt. No. FDA-2003-P-0273, at 45, <http://www.regulations.gov/#!documentDetail;D=FDA-2003-P-0273-0041> (last visited Feb. 15, 2012).

⁶² *Generic Drug Maze hearing*, *supra* note 40, at III.

⁶³ 153 CONG. REC. S5444, S5491 (2007).

⁶⁴ 21 U.S.C. § 355(q).

⁶⁵ Guidance for Industry, *Citizen Petitions and Petitions for Stay of Action Subject to Section 505(q) of the Federal Food, Drug and Cosmetic Act*, U.S. Department of Health and Human Services, Food and Drug Administration Center for Drug Evaluation, Jan. 2009, Dkt. No. FDA-2009-D-0008 at 1, <http://www.regulations.gov/#!documentDetail;D=FDA-2009-D-0008-0002> [hereinafter *Guidance for Industry*].

⁶⁶ Section 505(q)(1)(A). 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. Second, it does not cover petitions that “relate solely to the timing of approval” of a Paragraph IV application. Section 505(q).

⁶⁷ 153 CONG. REC. S11831, S11841 (2007).

⁶⁸ Guidance for Industry, *supra* note 65, at 2. It also applies to 505(b)(2) applications, which are viewed as “hybrids” containing more data than ANDAs but less than NDAs. Regulatory

ensure that they have not delayed filing the petition.⁶⁹ 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. Petitioners must certify that their allegations are true to the best of their knowledge and that they are not withholding unfavorable information.⁷⁰ Because the Act does not provide an opportunity for petitioners to cure the certification and verification requirements, it does not apply retroactively but only to petitions filed after enactment on September 27, 2007.⁷¹

Section 505(q) requires the FDA to 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 date.⁷² This period cannot be extended for any reason, even if the FDA finds that a delay in a related pending application is required.⁷³ 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 supplement to a petition was submitted with the primary purpose of delaying the approval of an application and the petition does not on its face raise any valid scientific or regulatory issues.”⁷⁴

The FDA released a Draft Guidance for Industry in 2009 to explain its interpretation of section 505(q).⁷⁵ The agency made clear that its analysis of delay would be interpreted expansively to apply to “any reasonable theory” of delay.⁷⁶

Professionals, Inc., *The 505(b)(2) New Drug Application – A Rapid Approval Route*, [http://www.regprofessional.com/resources/505\(b\)\(2\).pdf](http://www.regprofessional.com/resources/505(b)(2).pdf) (last visited May 25, 2012).

⁶⁹ 153 CONG. REC. S11831, S11841 (2007).

⁷⁰ Section 505(q)(1)(H).

⁷¹ *Id.*

⁷² Section 505(q)(1)(F).

⁷³ *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. Section 505(q)(2)(A); Guidance for Industry, *supra* note 65, 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. Section 505(q)(2)(B).

⁷⁴ Section 505(q)(1)(E).

⁷⁵ Guidance for Industry, *supra* note 65.

⁷⁶ *Id.*

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 methodology 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 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.⁷⁷

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.⁷⁸

In the regulations.gov database, citizen petitions take the form “FDA – year – P – four-digit number.”⁷⁹ 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

⁷⁷ 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 on www.regulations.gov. 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.

⁷⁸ 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 labeling issues), the agency could conclude that the drug is suitable for an ANDA.

⁷⁹ P denotes petition.

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 source 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 the petitions and accompanying FDA responses.⁸⁰ The Tracker confirmed the results we obtained through 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 of reviewing FDA rulings on citizen petitions involves the number of petitions that are not clear grants or denials. The FDA sometimes issues "mixed" decisions that 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.⁸¹

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 XL⁸² and Sanofi's insomnia drug Ambien,⁸³ several other examples demonstrate the 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.⁸⁴ 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

⁸⁰ "Citizen Petition Tracker," available on right margin at <http://www.fdalawblog.net/fda-law-blog-hyman-phelps/> (last visited Feb. 15, 2012).

⁸¹ The two authors independently made these determinations. They agreed on the outcome in 47 of 51 petitions. And they resolved the disputed 4 by consensus.

⁸² See *infra* notes 157-161 and accompanying text.

⁸³ See *infra* note 175 and accompanying text.

⁸⁴ FDA response to Purdue Pharmaceuticals Citizen Petition, Dkt. No. FDA-2007-P-0003 at 1-2, <http://www.regulations.gov/#!documentDetail;D=FDA-2007-P-0003-0009> (last visited Feb. 15, 2012).

alcohol dissolution tests.”⁸⁵ As a result, the agency “granted in part” the petitions “to the extent that they request actions we have already taken or are taking.” At the same time, it denied “the remaining requests.”⁸⁶

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 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.⁸⁷ 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.⁸⁸ 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 blood-pressure drug Cardine I.V. In that case, EKR asked the FDA to strip Teva of its NDA for the product, to refuse to allow it 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.⁸⁹

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.⁹⁰ 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.⁹¹

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

⁸⁵ *Id.* at 4.

⁸⁶ *Id.* at 12.

⁸⁷ *FDA response to Sanofi-Aventis Citizen Petition*, Dkt. No. FDA-2006-P-0025, at 2, <http://www.regulations.gov/#!documentDetail;D=FDA-2006-P-0025-0017> (last visited Feb. 15, 2012).

⁸⁸ *Id.* at 9.

⁸⁹ *FDA response to EKR Therapeutics Citizen Petition*, Dkt. No. FDA-2008-P-0621, <http://www.regulations.gov/#!documentDetail;D=FDA-2008-P-0621-0006> (last visited Feb. 15, 2012).

⁹⁰ *Id.*

⁹¹ *Id.*

approval process for NDAs or ANDAs. For example, Salix Pharmaceuticals filed several petitions relating to the drug Colazal, which treats ulcerative colitis.⁹² The petitions asked the FDA to not approve ANDAs without additional tests and to draft industry guidance on bioequivalence standards.⁹³

The FDA granted in part and denied in part the petition.⁹⁴ 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.⁹⁵

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.⁹⁶ 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.⁹⁷

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, even 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.⁹⁸

⁹² *FDA response to Salix Pharmaceuticals Citizen Petition*, Dkt. No. FDA-2005-P-0314, at 2, <http://www.regulations.gov/#!documentDetail;D=FDA-2005-P-0314-0004> (last visited Feb. 15, 2012).

⁹³ *Id.*

⁹⁴ *Id.* at 1.

⁹⁵ *Id.* at 6, 11, 22, 25. The "varying nature" signified that "a single bioequivalence recommendation" was not appropriate.

⁹⁶ *Id.* at 21, 26.

⁹⁷ Drugs@FDA, FDA, <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.DrugDetails> (last visited Feb. 15, 2012).

⁹⁸ One example is provided by the petitions filed concerning the pain-relieving skin patch, Duragesic. *FDA Consolidated Response to ALZA Citizen Petition*, Dkt. No. FDA-2004-P-

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 had 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, with 22% filed by generics and 10% by other parties.⁹⁹

As required by the 2007 amendment,¹⁰⁰ the FDA has reported to Congress the number of 505(q) petitions, including those delayed.¹⁰¹ 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.

0465. Each of the petitions raised modestly different points (suggesting 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.*

⁹⁹ 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.

¹⁰⁰ 21 U.S.C. § 355(q)(3).

¹⁰¹ The FDA reported 2 ANDA applications delayed out of 21 505(q) petitions filed from 2007 to 2008; 1 ANDA application delayed out of 31 505(q) petitions filed between 2008 and 2009; and 1 ANDA application delayed out of 20 505(q) petitions filed between 2009 and 2010. Public Law 110-85, *Annual Report on Delays in Approvals of Applications Related to Citizen Petitions and Petitions for Stay of Agency Action*, U.S. Department of Health and Human Services, Food and Drug Administration, Mar. 2008, at 3, available at <http://www.hpm.com/pdf/FDA%20FY2008%20505q%20CP%20Report.PDF>; Public Law 110-85, *Annual Report on Delays in Approvals of Applications Related to Citizen Petitions and Petitions for Stay of Agency Action*, U.S. Department of Health and Human Services, Food and Drug Administration, 2009, at 3, available at <http://www.hpm.com/pdf/FDA%20FY2009%20505q%20CP%20Report.PDF> [hereinafter 2009 Report]; Public Law 110-85, *Annual Report on Delays in Approvals of Applications Related to Citizen Petitions and Petitions for Stay of Agency Action*, U.S. Department of Health and Human Services, Food and Drug Administration, 2010, at 3, available at <http://www.hpm.com/pdf/blog/FDA%20FY2010%20505q%20CP%20Report.PDF>.

	Total	Brand Filer	Generic Filer	Other/ Uncategorized
2001	10	4	4	2
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 2/3 of petitions filed by brand firms.

	Brand v. Brand	Brand v. Generic	Brand v. Other¹⁰³
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,¹⁰⁴ 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 label concerns, and 31% advance other reasons.¹⁰⁵

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 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

¹⁰² Some percentages in Table 2 (and the other Tables in this Article) do not equal 100 due to rounding.

¹⁰³ The "other" category here represents those petitions for which the target of the petition was unascertainable.

¹⁰⁴ The Orange Book is an FDA publication that contains patents that brand firms believe would be infringed by generics. *Approved Drug Products with Therapeutic Equivalence Evaluations*, ELECTRONIC ORANGE BOOK (2012), <http://www.fda.gov/cder/ob/>.

¹⁰⁵ Petitions that fell into multiple categories were counted in each of the categories.

response (most typically, where the response does not appear on the regulations.gov website).¹⁰⁶

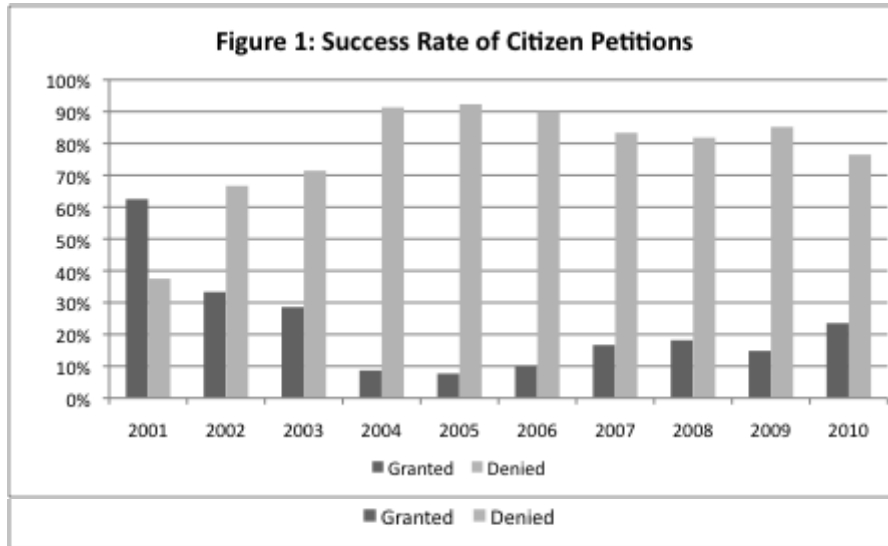


Table 3 presents these results in table form.

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%)	161¹⁰⁷

¹⁰⁶ There is no evidence that including petitions currently pending would have materially changed our results given how few petitions were pending and how similar the issues are in these petitions.

¹⁰⁷ 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.

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 8 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%.¹⁰⁸

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 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.¹⁰⁹

The conclusions in the Appendix are similar. Figure 1A provides the "Original Success Rate," in other words, the results 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 7 years, it fluctuated between 0% and 16%, with a mean of 8% and median of 8%. During these 7 years, the mean and median denial rates, respectively, were 92% and 92%.¹¹⁰

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. As the data accompanying Figure 2 (set forth in the margin) reveal, the FDA granted 22 petitions filed by brands, roughly 19%. And the agency denied 96 petitions, roughly 81%.¹¹¹

¹⁰⁸ See *supra* Tbl. 3 (comparing average of grants and denials from 2008 to 2010 to average of grants and denials from 2005 to 2007).

¹⁰⁹ There were a total of 16 truly mixed decisions (e.g., 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).

¹¹⁰ The denial rate of 81% in the text is modestly lower than the 85% figure appearing in App. Tbl. 3A since denials made up only 66% of the mixed decisions that were effectively grants or denials, less than the 85% of clear denials.

¹¹¹ For the years between 2001 through 2010, the FDA granted brand petitions 1, 2, 4, 2, 1, 1, 3, 3, 1, and 4 times for a total of 22. The agency denied petitions 2, 4, 9, 13, 9, 8, 12, 14,

Generics file fewer petitions. But their success rate is higher. As the data in the margin reveal, the FDA granted 8 (28%) petitions and denied 21 (72%) of petitions filed by generics.¹¹² In other words, generics enjoyed almost double the success rate of brands in filing petitions.

The number of brand petitions filed after the 2007 amendment did not decrease. To the contrary, in the three years before the amendment went into effect, there were 38 brand filings.¹¹³ In the three years after, there were 55, an increase of 45%.¹¹⁴

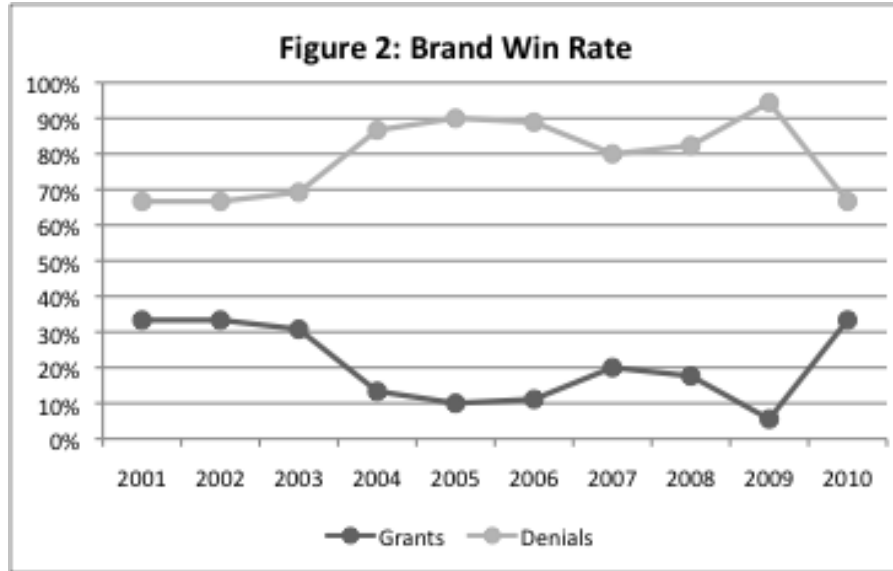
17, and 8 times for a total of 96. The total numbers in this section are lower than those in Tables 1 and 2 because of the requirement here of petitions followed by a substantive FDA response.

¹¹² 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.

¹¹³ In 2005, 2006, and 2007, there were 1, 1, and 3 grants; 9, 8, and 12 denials; and 0, 3, and 1 mixed decisions for a total of 38 petitions.

¹¹⁴ In 2008, 2009, and 2010, there were 3, 1, and 4 grants; 14, 17, and 8 denials; and 0, 3, and 5 mixed decisions 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. And in each of the three petitions, the FDA concluded that at least one of the studies requested was necessary, but the rest were not.



5. Brand win rate against generics

Brands file petitions against not only generics but also other brand firms. Figure 3 provides the brand success rate against generics. As the data accompanying Figure 3 (set forth in the margin) reveal, the FDA granted 18 petitions filed by brands against generics, roughly 20%. During this period, the agency denied 74 petitions, roughly 80%.¹¹⁵

Although the focus has generally been on brand petitions against 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 exclusivity¹¹⁶).

Brands file fewer petitions against other brands than against generics. But their success rate is higher. As the data in the margin show, the FDA granted 3 (37%) petitions against other brands and denied 5 (63%).¹¹⁷

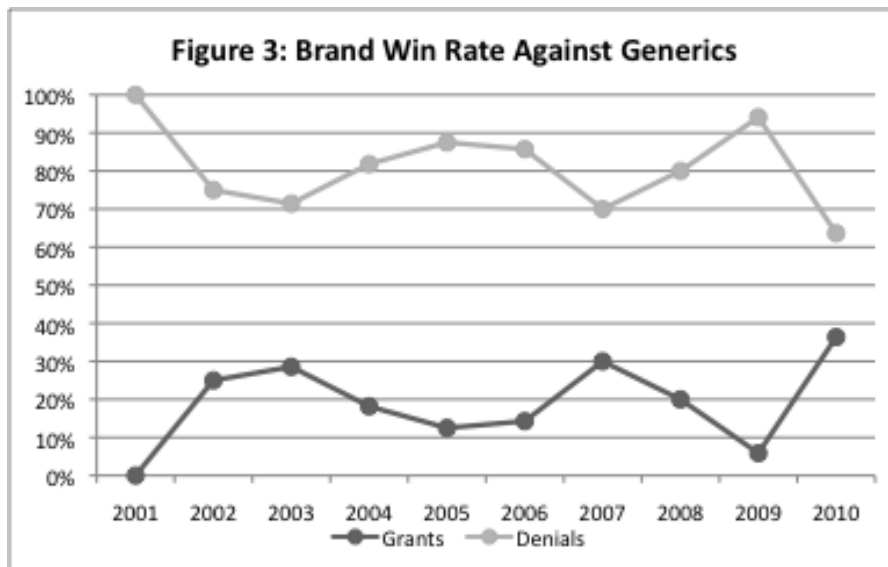
¹¹⁵ From 2001 through 2010, the number of grants each year for brand petitions against generics was 0, 1, 2, 2, 1, 1, 3, 3, 1, and 4, for a total of 18. The number of denials for brand petitions against generics was 2, 3, 5, 9, 7, 6, 7, 12, 16, and 7, for a total of 74. (Eight of the petitions were “mixed.”) 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.

¹¹⁶ Pediatric exclusivity refers to a six-month period of marketing exclusivity for companies conducting studies on children. 21 U.S.C. § 355a (2009).

¹¹⁷ From 2001 through 2010, brands obtained 3 grants against other brands (1 in 2002 and 2 in 2003) and 5 denials (3 in 2003 and 2 in 2007). Brands filed 22 petitions against unascertained targets, obtaining 1 grant, 17 denials, and 4 mixed decisions.

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.¹¹⁸ In the three years after, there were 47. In other words, the number of brand petitions against generics increased 68%, from roughly 9 to 16 each year.¹¹⁹

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.¹²⁰ In the following three years, the FDA granted 19% and denied 81% of brand petitions against generics.¹²¹



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

¹¹⁸ In 2005, 2006, and 2007, there were 1, 1, and 3 grants; 7, 6, and 7 denials; and 0, 2, and 1 mixed decisions for a total of 28 petitions.

¹¹⁹ In 2008, 2009, and 2010, there were 3, 1, and 4 grants; 12, 16, and 17 denials; and 0, 0, and 4 mixed decisions for a total of 47 petitions.

¹²⁰ In 2005, 2006, and 2007, the FDA granted 1, 1, and 3 (5 total) petitions filed by brands against generics while denying 7, 6, and 7 (20 total) petitions.

¹²¹ In 2008, 2009, and 2010, the FDA granted 3, 1, and 4 (8 total) petitions filed by brands against generics while denying 12, 16, and 7 (35 total) petitions.

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 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 even grant the petition for generic entry to be delayed. Even if the petition ultimately is denied, each day of postponed competition could be worth literally millions of dollars to the brand firm.

Citizen petitions cost little to the companies.¹²² 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.¹²³ Questionable petitions create a backlog at the FDA, which in turn hinders the other administrative tasks the agency is charged with, such as approving those ANDAs of other companies.¹²⁴

Just to pick one example, the FDA took 7 years to respond to Aventis's 2003 petition against generic Lovenox, issuing a 45-page answer in 2010 that responded to not only the petition but also Aventis's 12 supplements and comments filed between 2004 and 2009.¹²⁵

¹²² U.S. Food & Drug Administration, *Comment on Regulations: Making Your Voice Heard at FDA: How to Comment on Proposed Regulations and Submit Petitions*, Feb. 7, 2008, <http://www.fda.gov/AboutFDA/ContactFDA/CommentonRegulations/default.htm>.

¹²³ *Generic Drug Maze hearing*, *supra* note 40, at 70 (testimony of Heather Bresch).

¹²⁴ *Id.* at 51 (testimony of Gary Buehler). 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 (testimony of Heather Bresch).

¹²⁵ *FDA response to Aventis Pharmaceuticals Citizen Petition*, Dkt. No. FDA-2003-P-0273, <http://www.regulations.gov/#!documentDetail:D=FDA-2008-P-0621-0006> (last visited Feb. 15, 2012).

“Eleventh hour” petitions, or petitions filed within 6 months of patent expiration, are particularly tempting in forcing the FDA to take the time and resources to evaluate the merits of each filing, delaying generic approval.

At the same time, citizen petitions are costly for the generic, which is forced to invest resources in new studies, attempts to design around patents, and legal costs.¹²⁶ This process can be expensive, and if done too quickly, can compromise safety and efficacy.

2. Role in toolkit

In addition, citizen petitions can be used in combination with other activities to delay generic entry. For starters, they often 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 market before the end of the patent term.¹²⁷ 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.¹²⁸ 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.

For example, Biovail used a number of strategies to delay entry of a generic version of its best-selling anti-depression drug Wellbutrin XL. As discussed more fully below,¹²⁹ 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.¹³⁰

Nor is this example unique. In addition to the Wellbutrin, Ambien, and OxyContin cases discussed below,¹³¹ 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.¹³² Even though – less than one month later – a court found Alza’s patent to be invalid and not infringed, the brand was able to prevent generic competition for an additional 13 months, receiving an extra \$1.8 million each day its petition blocked generic

¹²⁶ *Id.* at 70 (testimony of Heather Bresch).

¹²⁷ 21 U.S.C. §355(j)(2)(A)(vii)(IV).

¹²⁸ 21 U.S.C. §355(j)(5)(B)(iii).

¹²⁹ *See infra* Section IV.A.

¹³⁰ *Meijer, Inc. v. Biovail Corp.*, No. CIV.A.08-2431=T, 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.

¹³¹ *See infra* Part IV.

¹³² *Generic Drug Maze hearing*, *supra* note 40, at 60 (testimony of Heather Bresch).

entry.¹³³

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.¹³⁴ 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 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 demonstrated 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."¹³⁵ And it has lamented that many petitions "involve[] theoretical arguments offered without full knowledge of the data actually submitted in the ANDAs."¹³⁶

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.¹³⁷

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.¹³⁸ The agency found that 50% of petitions filed between 2004 and 2006 to block generic entry

¹³³ Yael Waknine, *First-Time Generic Approvals: Ditropan XL, Zofran Injection/Premixed Injection, Oxandrin*, MEDSCAPE NEWS, Dec. 15, 2006, <http://www.medscape.com/viewarticle/549478>; U.S. Senate Special Committee on Aging, *Kohl, Leahy Introduce Bill To Stop Frivolous Citizen Petitions, Speed Generic Drug Approval*, Sept. 28, 2006, <http://aging.senate.gov/record.cfm?id=268246>.

¹³⁴ *Generic Drug Maze hearing*, *supra* note 40, at 69-70 (testimony of Heather Bresch, Senior Vice President of Corporate Strategic Development office of the CEO, Mylan Laboratories, Inc.).

¹³⁵ Dept. of Health & Human Servs., FDA, *Encouraging Early Submission of Citizen Petitions and Petitions For Stay of Agency Action*, Feb. 2009, at 3, available at <http://www.hpm.com/pdf/FDA%202009%20505q%20CP%20Report%20to%20Congress.PDF>.

¹³⁶ *Id.*

¹³⁷ Seth C. Silber et al., *Abuse of the FDA Citizen Petition Process: Ripe for Antitrust Challenge?*, 25 ANTITRUST HEALTH CARE CHRONICLE 26, 39 (Jan. 2012).

¹³⁸ HHS, *Encouraging Early Submission*, *supra* note 135, at 3.

raised issues regarding bioequivalence “long after ANDA applicants ha[d] conducted their bioequivalence studies.”¹³⁹

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 business, consumers, and taxpayers” by “allowing needed competition to bring down prices in the pharmaceutical market.”¹⁴⁰

The new policy requires the FDA to respond to 505(q) petitions within 180 days of a petition’s submission.¹⁴¹ 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.”¹⁴²

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.¹⁴³ In addition, the number of brand petitions against generics increased 68%, from 9 to 16 each year. And brands’ success rate against generics declined marginally from 20% before the amendment to 19% after.¹⁴⁴

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.”¹⁴⁵ 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.”¹⁴⁶ 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.”¹⁴⁷

¹³⁹ *Id.* at 4.

¹⁴⁰ 153 CONG. REC. S5454 (daily ed. May 2, 2007) (statement of Sen. Stabenow).

¹⁴¹ 21 U.S.C. § 355(q)(1)(F); Guidance for Industry, *supra* note 65, at 3.

¹⁴² 21 U.S.C. § 355(q)(1)(A)(ii); Guidance for Industry, *supra* note 65, at 11.

¹⁴³ *See supra* note 98 and accompanying text.

¹⁴⁴ *See supra* note 121 and accompanying text.

¹⁴⁵ Dept. of Health & Human Services, FDA, *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 6 (June 2011).

¹⁴⁶ *Id.*

¹⁴⁷ *Id.*

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.”¹⁴⁸

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. 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 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).¹⁴⁹ Wellbutrin entered the market in 2004 with annual sales of nearly \$1 billion.¹⁵⁰

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.¹⁵¹ Biovail then sued two of the four generics, Anchen and

¹⁴⁸ *Proposed FDA Rule Would Amend Citizen Petition Regulations*, REGULATORYFOCUS, Jan. 3, 2012, <http://www.raps.org/focus-online/news/news-article-view/article/563/proposed-fda-rule-would-amend-citizen-petition-regulations.aspx>.

¹⁴⁹ Wellbutrin XL, eMedTV, <http://depression.emedtv.com/wellbutrin-xl/wellbutrin-xl.html> (last visited Feb. 15, 2012).

¹⁵⁰ *Pharmaceutical Sales 2004*, DRUGS.COM, http://www.drugs.com/top200_2004.html (Feb. 15, 2012) [hereinafter *Top 200 Drugs by Sales 2004*].

¹⁵¹ Patent Nos. 6,096,341 & 6,143,327. *FDA Response to Biovail Corporation Citizen Petition*, Dkt. No. FDA-2005-P-0366/CP1 at 2, (originally FDA-2005-P-0498), <http://www.regulations.gov/#!documentDetail;D=FDA-2005-P-0366-0004> (last visited Feb. 15, 2012) [hereinafter *FDA Response to Biovail*]. 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. *Id.*

Abrika, for patent infringement. This suit, in December 2004, triggered a 30-month stay of ANDA approval under the Hatch-Waxman Act.¹⁵² 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 market.¹⁵³

On December 20, 2005, Biovail submitted a citizen petition requesting that the FDA not approve any ANDAs for generic versions of Wellbutrin XL.¹⁵⁴ 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.¹⁵⁵ The petition requested that ANDAs prove bioequivalence to not only Wellbutrin XL, but also the previous version of the drug, sustained-release Wellbutrin SR.¹⁵⁶

On August 1, 2006, a district court found that Anchen did not infringe Biovail's patent.¹⁵⁷ This finding of noninfringement ended Biovail's 30-month stay of FDA. But because of – and only because of – Biovail's citizen petition, 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.¹⁵⁸ Formally, the petition was granted in part, and denied in part.¹⁵⁹ 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.¹⁶⁰

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.¹⁶¹ 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

¹⁵² *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.

¹⁵³ *Id.* at 150.

¹⁵⁴ *Id.* at 151; *Biovail Citizen Petition*, Dkt. No. FDA-2005-P-0498/CP1.

¹⁵⁵ *Biovail Citizen Petition*, *supra* note 154, at 4.

¹⁵⁶ *Id.*

¹⁵⁷ *Biovail Labs. v. Anchen Pharms.*, 463 F. Supp. 2d 1073, 1077-78 (C.D. Cal. 2006).

¹⁵⁸ *FDA Response to Biovail*, *supra* note 151.

¹⁵⁹ *Id.*

¹⁶⁰ *Id.*

¹⁶¹ *Id.*

“dose dumping” information,¹⁶² which the FDA was already requiring from ANDA applicants.¹⁶³

In addition, the FDA made 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.”¹⁶⁴

On December 14, 2006, the same day the FDA responded to Biovail’s petition, the agency approved the first generic version of Wellbutrin XL, filed by Anchen Pharmaceuticals.¹⁶⁵

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.¹⁶⁶ 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.¹⁶⁷

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.¹⁶⁸ In the next two years, sales declined to roughly \$600 million and \$200 million, with less than 1 million units sold in 2009.¹⁶⁹

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

¹⁶² “Dose dumping” refers to the release of a drug faster than expected. *Medicinal Products Susceptible to ‘Dose Dumping’ Should Be Fully Tested*, PHYSORG.COM, Sept. 23, 2009, <http://www.physorg.com/news172934081.html>.

¹⁶³ *FDA Response to Biovail*, *supra* note 151.

¹⁶⁴ *FDA Response to Biovail*, *supra* note 151, at 16; *see Silber et al.*, *supra* note 164.

¹⁶⁵ Letter from Gary Buehler to Anchen Pharmaceuticals, Dec. 14, 2006, *available at* http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2006/077284s000ltr.pdf.

¹⁶⁶ *Pharmaceutical Sales 2006*, DRUGS.COM, http://www.drugs.com/top200_2006.html (last visited Feb. 15, 2012) [*hereinafter* Top 200 Drugs by Sales 2006] (apportioning 2006 sales of \$1,670,516 for the 133 days of delay).

¹⁶⁷ *Id.*

¹⁶⁸ *Pharmaceutical Sales 2007*, DRUGS.COM, http://www.drugs.com/top200_2007.html (last visited Feb. 15, 2012) [*hereinafter* Top 200 Drugs by Sales 2007].

¹⁶⁹ *Pharmaceutical Sales 2008*, DRUGS.COM, http://www.drugs.com/top200_2008.html (last visited Feb. 15, 2012) [*hereinafter* Top 200 Drugs by Sales 2008]; *Pharmaceutical Sales 2009*, DRUGS.COM, http://www.drugs.com/top200_2009.html (last visited Feb. 15, 2012) [*hereinafter* Top 200 Drugs by Sales 2009]; *Pharmaceutical Sales 2009*, DRUGS.COM, http://www.drugs.com/top200_units_2009.html (last visited Feb. 15, 2012) [*hereinafter* Top 200 Drugs by Units 2009].

The second example is provided by the insomnia drug Ambien.¹⁷⁰ In September 2005, the FDA approved Ambien CR, a controlled-release version of its bestselling drug Ambien (immediate release) IR.¹⁷¹ 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 IV certification, seeking to enter the market with a generic version of Ambien CR.¹⁷² 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."¹⁷³ 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.¹⁷⁴

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 petition technically 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 in finding that Anchen would not need to conduct additional studies.¹⁷⁵

In December 2010, two months after the FDA responded to the petition, Anchen's generic version of Ambien CR was approved.¹⁷⁶ In the period between June 7, 2007 (when Sanofi filed its petition) and October 13, 2010 (when the FDA ruled on the petition), Sanofi gained at least \$850 million in sales each year. From the 1,225-day delay resulting from the petition, Sanofi

¹⁷⁰ *FDA Response to Sanofi-Aventis Citizen Petition*, Dkt No. FDA-2007-P-0182 (originally 2007-P-0224), at 2, <http://www.regulations.gov#!documentDetail;D=FDA-2007-P-0182-0017> (last visited Feb. 15, 2012), [hereinafter *FDA Response to Sanofi-Aventis*].

¹⁷¹ *Id.*; *Ambien CR*, WIKINVEST, [http://www.wikinvest.com/stock/Sanofi-Aventis_SA_\(SNY\)/Ambien](http://www.wikinvest.com/stock/Sanofi-Aventis_SA_(SNY)/Ambien) (last visited Feb. 15, 2012).

¹⁷² Drugs@FDA, FDA, <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.LabelApprovalHistory#apphist> (last visited Feb. 15, 2012); Chih-Ming Chen, *Anchen Pharmaceuticals, Inc.: Its Past and Its Future*, Nov. 17, 2007, <http://rx.mc.ntu.edu.tw/alumni/epaper/16/01.pdf>.

¹⁷³ *FDA Response to Sanofi-Aventis*, *supra* note 170.

¹⁷⁴ *Id.*

¹⁷⁵ *Id.*

¹⁷⁶ *Par to Acquire Anchen Pharmaceuticals*, PHARMACEUTICAL NEWS, Sept. 26, 2011, <http://thepharmaceutical-news.com/par-to-acquire-anchen-pharmaceuticals>.

amassed more than \$3.1 billion in sales.¹⁷⁷

C. *OxyContin*

The third example is provided by Purdue Pharma's pain medication, OxyContin. 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 1995.¹⁷⁸

OxyContin was a blockbuster drug. In the early 2000s, it consistently grossed more than \$1 billion in sales, reaching \$1.8 billion in 2003.¹⁷⁹ On January 6, 2004, Purdue filed a stay of action petition, a request for the agency to refrain from approving any additional ANDAs for oxycodone.¹⁸⁰ Purdue asked the FDA to require all ANDA applicants to implement a risk-management program¹⁸¹ prior to marketing the drug and to include certain labeling information.¹⁸² The FDA denied the petition on March 23, 2004.¹⁸³

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.¹⁸⁴ After the generics entered the market, Purdue's OxyContin sales fell for the next three years, reaching \$680 million in 2006.¹⁸⁵

In 2006, the Federal Circuit overturned a lower court judgment, finding

¹⁷⁷ *Pharmaceutical Sales 2010*, DRUGS.COM, http://www.drugs.com/top200_2010.html (last visited Feb. 15, 2012) (\$742 million based on 285 days – Jan. 1, 2010 to Oct. 13, 2010 – of \$950 million annual sales); *Top 200 Drugs by Sales 2009*, *supra* note 169 (\$983 million annual sales); *Top 200 Drugs by Sales 2008*, *supra* note 169 (\$865 million annual sales); *Top 200 Drugs by Sales 2007*, *supra* note 168 (\$522 million based on 207 days – Jan. 1, 2007 to June 7, 2007 – of \$920 million annual sales).

¹⁷⁸ *FDA Response to Purdue Pharma L.P. Citizen Petition*, Dkt. No. FDA-2004-P-0245, at 2, (originally FDA-2004-P-0232), <http://www.regulations.gov#!documentDetail;D=FDA-2007-P-0245-0005> (last visited Feb. 15, 2012) [*hereinafter* *FDA Response to Purdue Pharma*].

¹⁷⁹ *Pharmaceutical Sales 2003*, DRUGS.COM, http://www.drugs.com/top200_2003.html (last visited Feb. 15, 2012).

¹⁸⁰ *FDA Response to Purdue Pharma*, *supra* note 178, at 1.

¹⁸¹ 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, and “surveillance and intervention for misuse, abuse, addiction, diversion, and overdose and other related serious events.” *Id.* at 3.

¹⁸² *Id.*

¹⁸³ *FDA Response to Purdue Pharma Petition for Stay*, Dkt. No. FDA-2004-P-0006 at 1, <http://www.regulations.gov#!documentDetail;D=FDA-2004-P-0473-0002> (last visited Feb. 15, 2012) [*hereinafter* *FDA Response to Purdue Pharma's Stay*].

¹⁸⁴ *Id.* at 2.

¹⁸⁵ *Top 200 Drugs by Sales 2006*, *supra* note 166.

that ANDA filers Endo and Teva had infringed Purdue's patent.¹⁸⁶ As a result, the generics left the market, which was followed by OxyContin sales in excess of \$1 billion.¹⁸⁷

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 Purdue's early petition for stay.¹⁸⁸

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.¹⁸⁹

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 long overdue.

After studying every petition filed between 2001 and 2010, this Article has concluded that petitions have increased in the past decade. Brand firms file most (68%) of the petitions, with more than 3/4 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 brands' 19% grant and 81% denial rates.

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 by 68% (from 9 to 16 per year).

¹⁸⁶ *Purdue Pharma L.P. v. Endo Pharms., Inc.*, 438 F.3d 1123 (Fed. Cir. 2006).

¹⁸⁷ Top 200 Drugs by Sales 2008, *supra* note 169.

¹⁸⁸ *FDA Response to Purdue Pharma*, *supra* note 178, at 2.

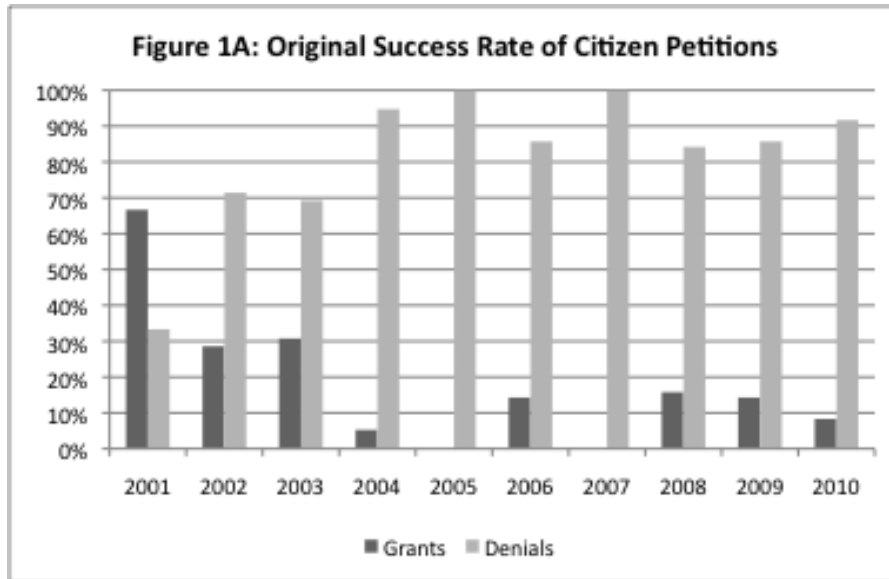
¹⁸⁹ Top 200 Drugs by Sales 2010, *supra* note 177 (OxyContin's 2010 total sales of \$3.55 billion).

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.

APPENDIX

	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%)

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



	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

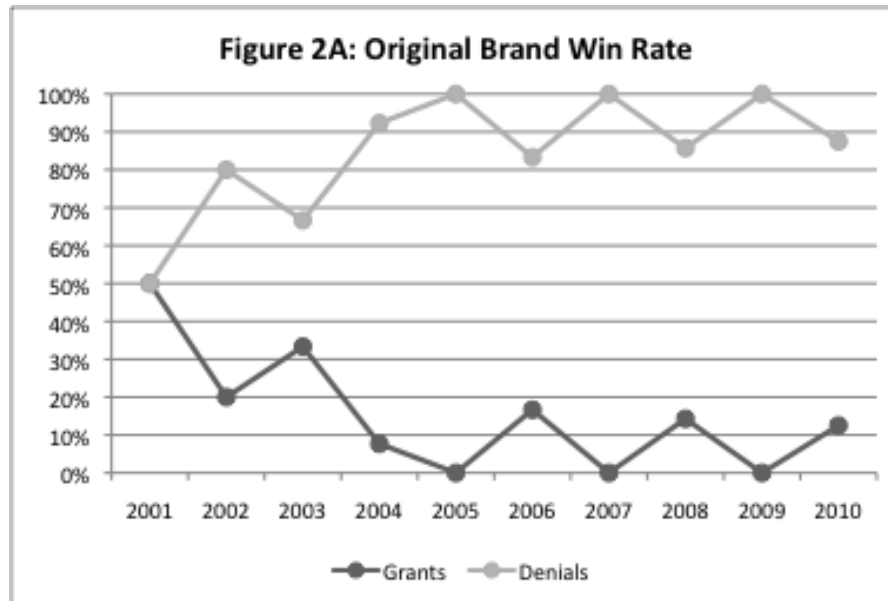


Figure 2A is similar to Figure 2 presented above. It differs by taking the FDA's grants and denials at face value. In other words, it does not parse the mixed decisions to determine if they are effectively grants or denials.

The data accompanying Figure 2A are set forth in the margin.¹⁹⁰ The FDA granted brand petitions 11 times (8%), denied them 78 times (60%), and reached mixed decisions in 41 (32%) cases. Focusing only on the cases in which the FDA granted and denied brand petitions, there were 12% grants and 88% denials. Generics encountered more success. As the data set forth in the margin reveals, there were 8 grants (24%), 19 denials (58%), and 6 mixed (18%) cases.¹⁹¹

¹⁹⁰ From 2001 through 2010, the FDA granted brand petitions 1, 1, 4, 1, 0, 1, 0, 2, 0 and 1 times for a total of 11. It denied brand petitions 1, 4, 8, 12, 6, 5, 10, 12, 13, and 7 times for a total of 78. And it reached mixed decisions in 2, 1, 1, 2, 4, 6, 6, 3, 8, and 8 cases for a total of 41. This total of 130 brand petitions matches the 118 discussed in connection with Table 3 (*see supra* note 111), once the 12 truly mixed decisions are included.

¹⁹¹ 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; 3 times in 2007, 2009, and 2010; 2 times in 2004 and 2005; and 1 time in 2002 and 2003 for a total of 19. There was 1 mixed decision in 2002 and 2010, and 4 mixed decisions in 2007, for a total of 6. These figures match the figures discussed in connection with Table 3 (*see supra* note 112). Focusing only on the cases in which the FDA granted and denied generic petitions, there were 30% grants and 70% denials.

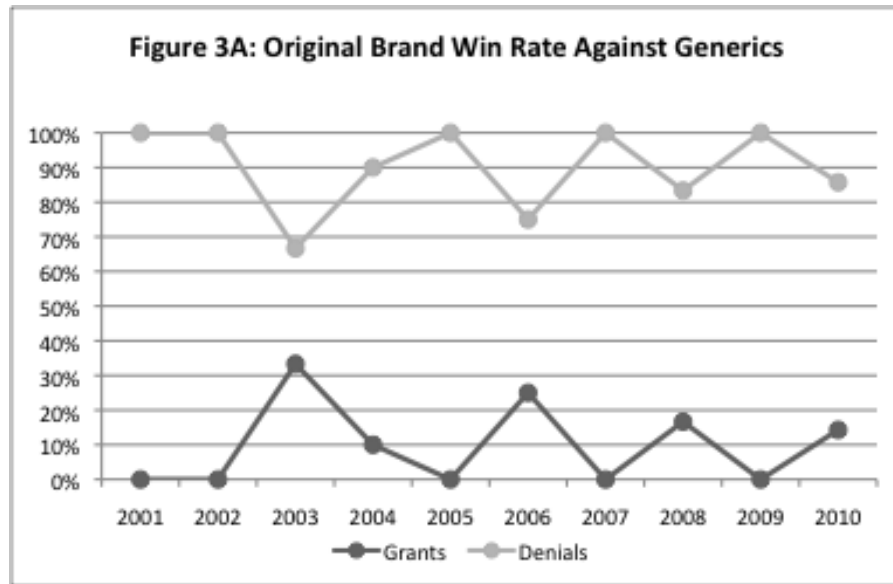


Figure 3A is similar to Figure 3 presented above. Like Figure 2A, it differs by taking the FDA's grants and denials at face value. The FDA granted brand petitions against generics 7 times (7%), denied them 58 times (58%), and reached mixed decisions in 35 (35%) cases.¹⁹² Focusing only on the cases in 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 (38%) and denied them 5 times (62%).¹⁹³

¹⁹² 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).

¹⁹³ 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).